Cornell University

Graduate School of Medical Sciences

Catalog 1993–1994

Academic Calendar 1993–94

1993

Orientation for new students	Wednesday, August 25–Thursday, August 26
Opening Exercises	Wednesday, August 25
Registration for **Quarter I*** and **Fall semester****	Thursday, August 26–Friday, August 27
Quarter I and **Fall semester** begin	Monday, August 30
Labor Day Holiday observed	Monday, September 6
Quarter I ends	Friday, October 22
Examinations for **Quarter I**	Friday, October 22–Friday, October 29
Registration for **Quarter II***	Friday, October 29 and Monday, November 1
Quarter II begins	Monday, November 1
Thanksgiving recess	Thursday and Friday, November 25 and 26
Winter recess: Instruction suspended 5:00 p.m.	Friday, December 17

1994

Winter recess ends: Instruction resumed 9:00 a.m.	Monday, January 3
Quarter II and **Fall semester** end	Wednesday, January 12
Last day for completing requirements for January degrees	Friday, January 14
Conferral of January degrees	Monday, January 17
Examinations for **Quarter II**	Thursday, January 13–Friday, January 24
Martin Luther King, Jr.'s Birthday observed	Monday, January 17
Registration for **Quarter III*** and **Spring semester*****	Friday, January 21 and Monday, January 24
Quarter III and **Spring semester** begin	Monday, January 24
Presidents' Day Holiday observed	Monday, February 21
Last day for registering for participation in Commencement	Friday, February 25
Quarter III ends	Friday, March 18
Examinations for **Quarter III**	Monday, March 21–Friday, March 25
Spring recess	Monday, March 28–Friday, April 1
Registration for **Quarter IV**	Friday, April 1 and Monday, April 4
Quarter IV begins	Monday, April 4
Fourteenth Annual Vincent duVigneaud Memorial Research Symposium; no classes	Wednesday, May 4
Last day for completing requirements for May degrees	Friday, May 20
Commencement Day, conferral of May degrees, 5:00 p.m., Avery Fisher Hall	Thursday, May 26
Quarter IV and **Spring semester** end	Friday, May 27
Memorial Day Holiday observed	Monday, May 30
Examinations for **Quarter IV**	Tuesday, May 31–Friday, June 3

Summer Term 1994

Summer research term begins	Monday, June 20
Summer research term ends	Friday, August 12
Last day for completing requirements for August degrees	Friday, August 19
Conferral of August degrees	Monday, August 22

Fall Semester 1994 (Projected)

Orientation for new students	Wednesday, August 24–Thursday, August 25
Opening Exercises	Wednesday, August 24
Registration for Quarter i* and Fall semester**	Thursday, August 25–Friday, August 26
Quarter I and Fall semester begin	Monday, August 29
Labor Day Holiday observed	Monday, September 5

* for students enrolling in courses.

** for students conducting research only, who are on leave of absence, or who are *in absentia*.

*** for students changing from course work to research, who are going on leave of absence, or who are converting to *in absentia* status.

Note: Courses are taught on a quarterly basis, degrees are granted at ends of the Fall and Spring semesters and of the Summer term. The dates shown in the calendar are subject to change at any time by official action of Cornell University.

In enacting this calendar, the Graduate School of Medical Sciences has scheduled classes on religious holidays. It is the intent of the school that students missing classes due to the observance of religious holidays be given ample opportunity to make up work.

Cornell University

Graduate School of Medical Sciences 1993 • 1994

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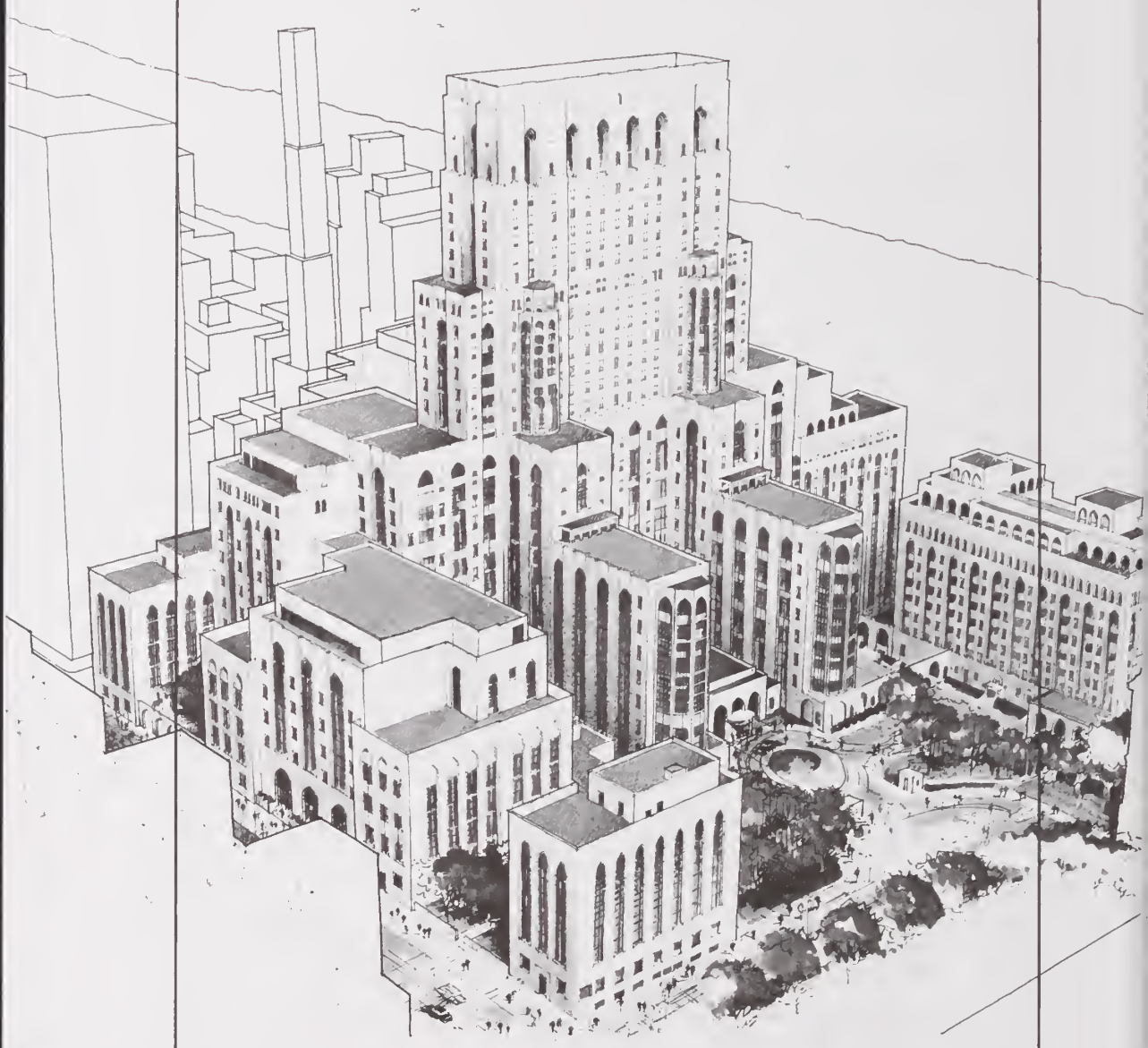
Editor/Coordinator: Carolyn B. Schnall

Contents

The courses and curricula described in this Catalog, and the teaching personnel listed herein, are as of July 1, 1993 and are subject to change at any time by official action of the Cornell University Graduate School of Medical Sciences.

New York Hospital–Cornell Medical Center



Cornell University
Graduate School of Medical Sciences

Purpose

The Graduate School of Medical Sciences, a semi-autonomous component of the Graduate School of Cornell University, provides opportunities for advanced study and research training in specific areas of the biomedical sciences. Graduate training leading to the degree of Doctor of Philosophy is offered by the following programs of study: *Biochemistry, Cell Biology and Genetics, Immunology, Molecular Biology, Neuroscience, Pharmacology, and Physiology and Biophysics.* Certain of these fields of study also offer programs leading to the degree of Master of Science. Collaborative programs with Cornell University Medical College lead to the combined degrees of Doctor of Philosophy and Doctor of Medicine.

The faculty of the Graduate School of Medical Sciences recommends the award of advanced general degrees not only as the result of the fulfillment of certain formal academic requirements, but also as evidence of the development and possession of a critical and creative ability in science. Demonstration of this ability is embodied in a dissertation which the candidate presents to the faculty as an original research contribution in the chosen area of study.

A close working relationship between student and faculty is essential to the program of the Cornell University Graduate School of Medical Sciences. Guidance for each student is provided by a Special Committee, a group of at least three faculty members selected by the student. This Special Committee is granted extraordinary independence in working with its student. Other than a broad framework of Graduate School of Medical Sciences requirements for residence, examinations, and a thesis, and additional requirements of the particular field of study chosen by the student, the Special Committee is free to design an individualized program of study with its students. No overall course, credit-hour, or grade requirements are set by the Graduate School of Medical Sciences. A student is recommended for a degree whenever the Special Committee judges the student qualified.

History

The opportunity for graduate study leading to advanced general degrees in the biomedical sciences was first offered at the Cornell University Medical College, in cooperation with the Graduate School of Cornell University, in 1912. In June of 1950, Cornell University, in association with the Sloan-Kettering Institute for Cancer Research, established additional opportunities for graduate study by forming the Sloan-Kettering Division of the Medical College. The resulting expansion of both graduate faculty and research training opportunities on the New York City campus prompted the organization in January, 1952 of the Graduate School of Medical Sciences, composed of two cooperative but separate divisions, known as the Medical College Division and the Sloan-Kettering Division. The Graduate School of Medical Sciences was given full responsibility for advanced general degrees granted for study in residence on the New York City campus of Cornell University.

Facilities

The Cornell University Graduate School of Medical Sciences is part of a large biomedical center extending along York Avenue between 65th and 72nd Streets on Manhattan's East Side. This complex includes Cornell University Medical College, New York Hospital, the Memorial Sloan-Kettering Cancer Center, and The Rockefeller University. The core facilities of the Graduate School of Medical Sciences, which include the research laboratories of its faculty, are located within the Cornell Medical College—New York Hospital complex and the Howard, Kettering, Rockefeller, and Schwartz Laboratory buildings of the Sloan-Kettering Institute for Cancer Research. Other buildings in this area provide student housing and recreational facilities. Several dining rooms and snack bars are located in this complex, and the immediate neighborhood abounds in a large variety of restaurants.

Especially noteworthy are two large biomedical libraries available to graduate students. The smaller of the two, the Medical Library—Nathan Cummings Center, contains over 33,500 books and journals. The Cornell University Medical College Library has a collection of 149,000 volumes and subscriptions to 1,500 journals. It is one of the country's first fully automated medical libraries featuring computer terminals which provide access to library materials and permit bibliographic searches in a number of data bases. A microcomputer center, with an extensive software collection, is maintained at the library for staff and students.

Organization

The faculty of the Graduate School of Medical Sciences is composed of the professional staffs of the basic science and clinical departments of Cornell University Medical College, and the professional staff members of the Sloan-Kettering Institute for Cancer Research.

Graduate training is offered in several areas of the biomedical sciences. These Programs of Study bring together faculty members who have related research and teaching interests.

Executive Committee

The Executive Committee is both the administrative and judicial board of the Graduate School of Medical Sciences and its members have continuing responsibility for the academic affairs of the school. The Committee is composed of the Chairpersons of the graduate programs, the Dean as chairperson, the Associate Dean, the Provost for Medical Affairs of Cornell University, the Chairperson or Vice-Chairperson of the Sloan-Kettering Institute, the Chairperson and Vice-Chairperson of the Faculty Advisory Committee (see below), and two non-voting, elected student representatives.

The Executive Committee considers such matters involving the interests and policies of the Graduate School of Medical Sciences as are referred to it by the Faculty Advisory Committee, by individual members of the Faculty, or are generated upon its own initiative. The Committee approves the addition or deletion of programs of study, reviews the admission of students, approves a student's major and minor programs, reviews the curriculum and requirements for degrees.

The Executive Committee is chaired by the Dean, who is the academic administrative officer of the Graduate School of Medical Sciences and is also an Associate Dean of the Graduate School of Cornell University. The Associate Dean, who is also an Assistant Dean of the Graduate School of Cornell University, is the Secretary of the Executive Committee.

Faculty Advisory Committee

The Faculty Advisory Committee is the primary body representing the views of the Faculty of the Graduate School of Medical Sciences. The Committee advises the Dean and the Executive Committee on the impact of educational and policy matters under their consideration and recommends changes in educational activities, procedures, and policy of the Graduate School of Medical Sciences.

The Faculty Advisory Committee is composed of the elected Program Directors and two elected student representatives. The Chairperson and Vice-Chairperson of the Committee are elected by its membership. Non-voting members are the Dean and Associate Dean, the Provost for Medical Affairs of Cornell University, and the Chairperson or Vice-Chairperson of the Sloan-Kettering Institute.

Special Programs

Tri-Institutional MD-PhD Program

This program offers a small number of highly qualified college graduates the opportunity to study both clinical and biomedical disciplines leading to the MD and PhD degrees. The combination of basic research skills and clinical experience prepares students in the program for teaching and investigative careers. Preclinical and clinical training are provided by the faculty of Cornell University Medical College. Research opportunities are offered in the laboratories of the Cornell University Graduate School of Medical Sciences, The Rockefeller University, and the Sloan-Kettering Institute.

The MD-PhD Program offers an intensive and intellectually challenging six-to-seven-year course of study. Participants spend the first two years as medical students mastering the preclinical sciences and attending research-oriented seminars led by experts in the biomedical fields. The summer months are spent in the laboratory learning experimental techniques and doing research. The students spend the next three to four years as full-time graduate students, mainly doing laboratory research and writing the thesis. Research training is offered in the following areas: biochemistry, cell and developmental biology, immunology, molecular biology and genetics, molecular pharmacology and therapeutics, neuroscience, physiology and biophysics, and virology and microbiology. The final year consists of required clerkships in medicine, surgery, obstetrics and gynecology, pediatrics, neurology, psychiatry, radiology, public health, and anesthesiology. The six-to-seven-year plan satisfies the minimum residency requirements for both the MD and PhD degrees.

A successful applicant will demonstrate excellent undergraduate science preparation and a strong commitment to combining an investigative career in the biomedical sciences with clinical medicine. Applicants must satisfy the requirements of each institution. All students accepted in the MD-PhD Program receive full-tuition scholarships and stipends to cover living expenses for the entire period.

For application to the MD-PhD Program, see p. 71.

PhD-MD Program

Students enrolled in the Graduate School of Medical Sciences may be eligible for admission into the PhD-MD Program, jointly sponsored by the Medical College and the Graduate School of Medical Sciences. This program is designed for those graduate students who find that their teaching and research goals require the acquisition of the MD degree in addition to the PhD degree. The program is *not* designed as an alternate path for students who have the MD degree as their primary goal, but who have not been accepted by a medical school. Those who know, at the time of application to Cornell, that they want to pursue a course of study leading to both degrees should apply to the MD-PhD program described above.

See p. 72 for application and graduation requirements of the PhD-MD program.

Faculty and Research Activities

Biochemistry

Faculty

Mary E. Anderson
John P. Blass
Adele L. Boskey
Esther M. Breslow
Arthur J.L. Cooper
Gordon F. Fairclough
Jack Goldstein
David P. Hajjar
Katherine A. Hajjar
Rudy H. Haschemeyer
Bernard L. Horecker (Emeritus)
Alton Meister (Emeritus; active)
Ursula Muller-Eberhard
Abraham Novogrodsky
Hugh D. Robertson
Albert L. Rubin
Anthony W. Scotto
Richard L. Soffer
Kurt H. Stenzel
Suresh S. Tate
Sidney Udenfriend
Daniel Wellner
David Zakim

Research Activities

Members of the Biochemistry program are engaged in research spanning a wide spectrum of scientific areas in which a variety of modern techniques of molecular biology and chemistry is used.

Dr. Anderson's research involves the synthesis of compounds which increase or decrease cellular glutathione levels. These inhibitors or prodrugs are used *in vitro, in vivo* or in culture to study the metabolism and function of glutathione. Enzyme studies include cloning, expression and site-specific mutagenesis to examine enzyme mechanisms. Recent research interests include the mechanisms of T lymphocyte activation, development of multi-drug resistance, the effects of viral infection on glutathione metabolism, and the role of thiols in nitroglycerin-mediated vasodilation.

Dr. Blass's research focuses on the neurochemistry of disease, and specifically on the cellular and molecular neurobiology of Alzheimer's disease. His laboratory concentrates on the use of cell culture models, including cultures developed in his laboratory from autopsy human brain. These models are used to study regulation and other dynamic aspects of cellular function which can not be studied in autopsy brain.

Dr. Boskey's research is concerned with elucidating the factors controlling physiologic and dystrophic calcification. Changes in the structural properties of bone mineral (hydroxyapatite) in normal and diseased tissues are studied using x-ray diffraction, and Fourier Transform infrared microscopy. Special emphasis is placed on analysis of changes in osteoporotic bones. Hydroxyapatite formation and growth are studied in solution, collagen gels, in animal tissues, and in cell culture. Recent studies have addressed the multiple roles matrix proteins play in regulating the properties of the mineral, the role of the cell in regulating extracellular mineral deposition, and the influence of vitamin D metabolites on the calcification process.

Dr. Breslow is concerned with understanding the forces that determine the specificity of protein-protein interactions and the relationship between protein structure and function. She has been studying the interactions of the pituitary peptide hormones, oxytocin and vasopressin, with their storage protein, neurophysin. Recent studies have led to the elucidation of the first X-ray crystal structure of a neurophysin complex.

Views of Manhattan from Cornell Medical College

Present work is focused on determining the mechanism by which the hormones guide the folding of the neurophysin chain, on the application of molecular mechanics to the analysis of the binding specificity of the neurophysins, and on the molecular mechanisms by which the binding of hormones to neurophysin influences its allosteric properties. A second area of research concerns the mechanism by which proteins are degraded intracellularly during normal protein turnover. The aims of these studies are to understand the precise role of ubiquitin, a small protein known to be involved in this process, and to elucidate the mechanisms underlying the selection of proteins for degradation.

Dr. Cooper's laboratory is working in the area of α-keto acid biochemistry and pyridoxal phosphate enzymes. Another area of active research is the metabolism of amino acids and ammonia in the brain and other tissues. For this purpose, molecules labeled with short-lived positron-emitting isotopes are synthesized, and their distribution in tissues is analyzed by various techniques including positron emission tomography. Cerebral energy metabolism and its disruption in various disease states are also being investigated as are possible metabolic defects in Alzheimer's disease. Dr. Cooper is also working on the design of specific enzyme inhibitors of two metabolically important enzymes, namely aspartate aminotransferase and lactate dehydrogenase. His group has isolated and is studying the molecular biology of an enzyme implicated in the bioactivation of certain nephrotoxic/cerebrotoxic halogenated compounds.

Dr. Goldstein is studying the structure and function of erythrocyte surface antigens and is working on enzymatic methods for the removal of immuno-dominant sugars responsible for blood group A and B activity. He is also isolating and characterizing proteins exhibiting Rh structures, clarification of the genetic systems involved in Rh expression and modification of such antigenic sites by chemical and enzymatic procedures.

The central focus of *Dr. David Hajjar's* program is to define the chemistry of lipids as they relate to their accumulation in arteries during atherosclerosis. Dr. Hajjar has directed his efforts to the exploration of structure-function relationships involved in the regulation of cholesterol metabolism. Techniques used in the laboratory to study substrate-enzyme metabolic interactions include site-directed mutagenesis and differential scanning calorimetry.

Dr. Katherine Hajjar's laboratory is investigating cellular interactions involved in thromboregulation. A major focus is the interaction of plasminogen and tissue plasminogen activator with human endothelial cells. Upon activation, plasminogen forms plasmin, the major fibrinolytic enzyme in blood. Recent work has focused on the molecular identification and characterization of an endothelial cell membrane receptor which binds plasminogen as well as tissue plasminogen activator and appears to support the constitutive generation of plasmin. Binding of plasminogen to this receptor appears to be modulated by the atherogenic LDL-like particle, lipoprotein(a), while the receptor's interaction with tissue plasminogen activator is markedly reduced by the thiol amino acid, homocysteine. A second area of interest is the identification and characterization of a human hepatic lectin involved in clearance of tissue plasminogen activator from blood. Methods currently employed in the laboratory include tissue culture, subcellular fractionation, protein purification techniques, metabolic labeling and immunoprecipitation, Western and ligand blotting, Northern blotting, polymerase chain reaction, DNA transfection, and molecular cloning.

Dr. Haschemeyer's laboratory concentrates on the application of computer modeling methods to the study of macromolecular structure, biological flow, and heterogeneous-phase reactions. Additional computer applications are directed toward

defining prognostic factors and treatment protocols that optimize graft survival in kidney transplant patients.

Dr. Meister's research is concerned with the study of enzymes, especially those involved in amino acid and peptide metabolism. The research involves isolation of enzymes, determination of their structures and properties, cloning, sequencing and expression. The research is basic in nature, but significant relationships between this research and human disease have been discovered and are also being explored. Current work involves the metabolism and function of glutathione, including the relationships of this tripeptide to transport, metabolism, radiation, chemotherapy, and the functions of mitochondria and cells of the immune system.

Dr. Muller-Eberhard is investigating the mechanisms of transport of iron protoporphyrin IX and its metabolic precursors by proteins in the blood stream as well as within hepatocytes. She is studying the exchange of porphyrins between proteins purified from serum and from hepatocytes; developing methods which delineate the function of these proteins in the delivery of porphyrins to hepatocytes and their intracellular distribution; and assessing the interaction of these proteins with artificial and biological membranes to learn how they may facilitate ligand transport across cellular and intracellular barriers.

Dr. Robertson's work involves the structure and function of biologically active RNA molecules. Recent work has focused on RNA-catalyzed cleavage of viroid-like RNA pathogens, and the use of the ribozymes so isolated for the study of the replication of these agents, and in antiviral therapeutics. The ribozymes from the genomic and antigenomic RNA strands of the human delta hepatitis agent have recently been isolated and separated into enzyme and substrate components. Mechanistic studies on mutant wildtype ribozyme strands, which can be as short as 26 nucleotides in length, are under way, and re-targeting to allow these human liver-based activities to cleave other viral RNAs, particularly that of the hepatitis B virus, are being carried out. These studies use a variety of synthetic and analytical techniques aimed at discerning the chemical and physical structure, and the biological function, of the RNA molecules under study, and are conducted in collaboration with Dr. A. D. Branch, Rockefeller University.

Dr. Scotto's laboratory is working in the area of membrane biogenesis and liposome technology. The mechanism of the spontaneous insertion of membrane proteins into preformed bilayers is under study. Proteoliposomes formed by this process are being used as model membranes to explore membrane interactions of lipid-protein bilayers as an alternative to the liposome model. The results of these studies are now being applied to the formation of both polymer-modified and glycosylated proteoliposomes as stable drug delivery vehicles.

The main objective of *Dr. Soffer's* research is to characterize the physical, chemical, and biochemical properties of angiotensin II receptor which has been purified to a nearly homogeneous state from rabbit hepatic membranes.

Drs. Stenzel and Novogrodsky are interested in determining mechanisms involved in the regression of metastatic kidney tumor mediated by autologous killer cells activated by the oxidizing mitogens and recombinant interleukin 2 (rIL2). They are using *in vitro* systems to determine mechanisms of cell-mediated cytotoxicity. These investigations include an analysis of mononuclear cell sub-populations involved, mechanisms of target cell lysis (membrane structures *vs.* soluble factors), target specificity, and synergistic effects of additional biologic response modifiers. *In vivo* systems are used to determine mechanisms of tumor lysis *in vivo* mediated by administration of

activated killer cells and rIL2 in mouse tumor models. Clinical studies are under way in patients with metastatic renal cell carcinoma to determine efficacy and toxicity of adoptive immunotherapy. Alterations in patients' immune responses are determined. These studies include a structural and functional analysis of circulating mononuclear cell populations.

Dr. Tate is investigating the molecular basis of amino acid transport in animal cells. Amino acids are necessary not only for protein synthesis but also for the cell's energy metabolism and for the synthesis of neurotransmitters and other bioactive molecules. They are transported into mammalian cells by a number of carrier-mediated systems, and only recently have the proteins mediating such transport begun to be characterized at the molecular level. One of the first such carriers was cloned by Dr. Tate from rat kidney, employing the *Xenopus* oocyte expression system. This protein facilitates sodium-independent transport of neutral aliphatic and aromatic amino acids as well as cationic amino acids. It is localized primarily in the brush border membranes of epithelial cells of the kidney, intestine, etc. Current studies are aimed at elucidating the structure and function relationships in this transporter and at the molecular characterization of other amino acid transporters.

Dr. Wellner's laboratory is concerned with the structure and function of enzymes involved in amino acid metabolism, such as L-amino acid oxidase and threonine deaminase. Techniques employed for the study of protein structure include amino acid analysis and microsequencing using a gas-phase protein sequencer.

Dr. Zakim's research is focused on interactions between the apolar region of membrane lipids and molecules solvated by this region of biological membranes. The aspects of this broad problem that are being studied are (i) how lipids determine the function of integral membrane enzyme, and (ii) the factors determining the solubility of small hydrophobic molecules within the apolar region of bilayers. A variety of enzymological and physical techniques is used in this work, including calorimetry, infrared spectroscopy, and high pressure enzyme kinetics, to elucidate the effects of the lipid matrix on the structure and functional properties of solvated molecules, large and small, and to determine as well how the solvated molecules impact on the lipids.

Recent Publications

Anderson, M. E. (with Kalebic, T., Kinter, A., Poli, G., Meister, A., and Fauci, A. S.), Suppression of HIV expression in chronically infected monocytic cells by glutathione, glutathione ester, and N-acetyl cysteine. *Proc. Natl. Acad. Sci. USA* 88:986–990, 1991.

Anderson, M. E. (with Godwin, A. K., Meister, A., O'Dwyer, P. J., Huang, C-S., Hamilton, T. C.), High resistance to cisplatin in human ovarian cancer cell lines is associated with marked increase of glutathione synthesis. *Proc. Natl. Acad. Sci. USA* 89:3070–3074, 1992.

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Boskey, A. L. (with Stiner, D., Leboy, P., Doty, S., and Binderman, I.), Optimal conditions for cartilage calcification in differentiating chick limb-bud mesenchymal cells. *Bone & Min.* 16:11–37, 1992.

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Cooper, A. J. L. (with Lai, J. C. K.), Neurotoxicity of ammonia and fatty acids: differential inhibition of mitochondrial dehydrogenases by ammonia and fatty acyl coenzyme A derivatives. *Neurochem. Res.* 16:795-803, 1991.

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Goldstein, J. (with Suyama, K.), Membrane orientation of Rh(D) polypeptide and partial localization of its epitope-containing domain. *Blood* 79:808-812, 1992.

Hajjar, D. P. (with Nicholson, A. C.), TGF-ß upregulates LDL receptor-mediated cholesterol metabolism in arterial smooth muscle cells. *J. Biol. Chem.* 267:25,982-25,987, 1992.

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Hajjar, K. A. (with Etingin, O. R., Hajjar, D. P., Harpel, P. C., and Nachman, R. L.), Lipoprotein(a) regulates plasminogen activator inhibitor-1 expression in endothelial cells: a potential mechanism for thrombogenesis. *J. Biol. Chem.* 266:2459-2465, 1991.

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Cell Biology and Genetics

Faculty

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Neal Rosen
James E. Rothman
Roy L. Silverstein
Martin Sonenberg
Lisa Staiano-Coico
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Research Activities

The faculty of the Program in Cell Biology and Genetics conduct research in a broad range of fields which include the most exciting areas of genetics and cell-developmental and molecular biology. Specific interests include the developmental biology of the early embryo and of cardiovascular and muscle tissues; membrane biology; cell motility and the cytoskeleton; the molecular biology of cell growth, differentiation and oncogenic transformation; endocrinology and hormone receptors; human somatic cell and cytogenetics; molecular virology. These studies are pursued using the most current cell biological, genetic, molecular and immunological methodologies in modern and well-equipped facilities.

Dr. Bachvarova is interested in gene expression in early mouse embryos and germ cells. Current projects under investigation include: the control of translation of endogenous and injected mRNAs during meiotic maturation of mouse oocytes, the expression of genes encoding growth factors that may be involved in mesoderm induction, and the expression of c-*kit*, a tyrosine kinase receptor involved in germ cell development. *Dr. Bader's* laboratory is concerned with the commitment and differentiation of cardiac progenitor cells. The cellular and molecular controls of cardiac gene expression are of central interest. *Dr. Benezra's* research is focused on the newly discovered Id protein, a functional antagonist of the helix-loop-helix class of transcriptional activators. His interest is in the role of this transcriptional repressor in embryonic development and

muscle differentiation. *Dr. Biedler's* research concerns the genetic mechanisms underlying the cellular acquisition of multiple resistances to cancer chemotherapeutic agents. At least two amplified genes with a role in this process have been identified and are being studied. A second area of research is human neuroblastoma, a system involving amplification of a specific gene and consequent cytogenetic abnormalities. Current studies are focused on the correlation of the differential expression of the N-myc oncogene and the EGF receptor gene with varying states of malignant transformation and/or cell differentiation. *Dr. Blobel's* lab is studying the role of a new family of integrin ligands in fertilization and myogenesis. This new protein family is related to snake venom integrin ligands called disintegrins, and is implicated in cell-cell binding, fusion, and potentially in signaling.

Dr. Brown's laboratory is studying a family of genes (Wnt genes) encoding intercellular signaling molecules that function in both embryogenesis and tumorigenesis. A major focus is the protein product of the proto-oncogene Wnt-1 and its mechanism of action in cell culture systems. *Dr. Caudy* is interested in the molecular genetic mechanisms which control neuronal pattern formation during development. A network of cell determination genes which control neuronal cell fate in *Drosophila* embryos are the major focus of his laboratory. The proteins encoded by this gene family are members of the helix-loop-helix class of transcription factors, whose mammalian homologues are proto-oncogenes. The major aim of *Dr. Chaganti's* research is to define the role played by hereditary factors in the etiology and progression of human malignancy. Studies focus on inherited changes associated with cancer predisposition and with acquired changes associated with various tumors. Chromosomal rearrangement, gene amplification, point mutation and gene deregulation are considered. *Dr. Chao's* research interests focus on gene expression and regulation in mammalian cells. Molecular genetic techniques are being applied to study the gene encoding the nerve growth factor receptor and to analyze the role of the receptor in the mechanism of signal transduction by NGF and in the development of the nervous system.

The focus of *Dr. Citi's* research is the structure of tight junctions, which are critical for epithelial cell function. Biochemical and molecular genetic analysis of cingulin, a specific tight junction protein, is being undertaken to understand its role in the junction. A variety of research areas with relevance to human *in vitro* fertilization is the focus of the work in *Dr. Cohen's* laboratory. These include the development of improved micromanipulations which aid sperm in crossing the zona pellucida as well as approaches to correcting polyspermic embryos. Embryo co-culture and preimplantation genetic diagnosis are also topics of interest. *Dr. Fischman's* research focuses on the cell and molecular biology of skeletal and cardiac muscle development. The identification of genes encoding novel muscle components, retroviral analysis of cell lineages, and targeted gene insertions are being employed to better define the steps involved in sarcomere assembly. *Dr. Freedman's* laboratory is attempting to elucidate the molecular mechanisms by which DNA binding proteins affect differential gene expression. His work is centered on the study of transcription factors containing the important zinc finger motif and their direct role in mediating regulatory events which control development and differentiation. Several clinically relevant aspects of human genetics are under study in *Dr. German's* laboratory. The primary defect in Bloom's syndrome is being mapped with the eventual goal of cloning the gene involved; this syndrome illustrates the developmental consequences of somatic mutation. The molecular dissection of the pseudoautosomal and adjoining regions of human sex chromosomes is also an area of research interest.

The focus of research in *Dr. Gershengorn's* laboratory is the delineation of the mechanisms of signal transduction used by thyrotropin-releasing hormone (TRH) in pituitary cells. Using a recently isolated cDNA for the TRH receptor, the molecular details of TRH binding, of coupling to a G protein that activates inositol lipid hydrolysis, and of receptor regulation will be studied. *Dr. Gumbiner's* group is investigating the functions of cell adhesion molecules and intercellular junctions in tissue morphogenesis. The main emphases are the molecular mechanisms of cadherin function, including the roles of associated cytoplasmic proteins, and the role of cadherins and associated proteins in the early development of the frog *Xenopus laevis*. Research in *Dr. Hajjar's* laboratory focuses on the cellular portal of entry of herpesvirus and the role these viruses may play in the activation of the coagulation cascade on the surface of the blood vessel wall and the atherosclerotic process. The role of molecular chaperones in catalyzing the folding of newly synthesized polypeptides is the major focus of *Dr. Hartl's* research. How members of the hsp70 and hsp60 families direct protein folding and intracellular sorting is of specific interest. *Dr. Jaffe* is studying stimulus-response coupling, signal transduction, and prostacyclin production in endothelial cells. Current research includes expression cloning of the human endothelial cell thrombin receptor using the *Xenopus laevis* oocyte system. Cytokine-induced expression of endothelial cell surface antigens is also being studied. The focus of *Dr. Jasin's* work is the development of methods to precisely modify the mammalian genome by recombination. The mechanism by which mammalian cells achieve homologous recombination is also of interest. *Dr. Klein* is studying the effects of cardiac contractility and thyroid hormone on the regulation of cardiac myosin synthesis. The roles of gene expression in cell differentiation and mammalian development are the two major interests of *Dr. Lai*. The approaches taken in the laboratory include the identification and analysis of a novel family of transcription factors which control cell-specific gene expression. Of major interest to *Drs. Marks* and *Rifkind* are the cellular and molecular mechanisms that control coordinated gene expression and proliferation during induced cell differentiation. The principal experimental model is the murine erythroleukemia cell (MELC), which is a virally transformed red blood cell precursor arrested at a stage of the lineage called the colony-forming cell for erythropoiesis. A number of defined chemical agents can induce MELC to express the genetic program of erythroid differentiation. Present studies address the signal mechanisms triggered by inducing agents, the mechanism of induced gene expression, and the identification and cloning of genes implicated in the programmed cessation of cell proliferation.

Dr. Massagué's research interests concern the mediation of intercellular communication by growth and differentiation factors. Much of the research is centered on understanding the activities of transformation growth factors (TGF). The research within *Dr. Mikawa's* laboratory is focused on the molecular mechanisms involved in cardiac differentiation and morphogenesis. The major experimental approach involves the use of recombinant retroviruses to modulate the *in vivo* expression of genes encoding growth factors, cell adhesion proteins and *trans*-acting DNA binding proteins. *Dr. Moore's* research concerns the mechanism of action of hematopoietic growth factors and interleukins in regulating the proliferation and differentiation of normal and leukemic hematopoietic stem cells. The regulation of factor production and the modulation of receptors on various cell populations are being analyzed; *in vivo* tumor models are being investigated to test the potential for cytokine treatment in intensified chemotherapy. The focus of work in *Dr. Nachman's* laboratory is the endothelial cell membrane and the macromolecular assembly of fibrinolytic constituents that influence vascular non-thrombogenicity. *Dr. Nathan's* efforts are aimed at understanding how phagocytic leukocytes kill microbes, tumor cells, and normal host elements at inflammatory sites. Investigations into the biochemical bases of cytotoxicity by macrophages and granulocytes are integrated into a context of cell biology and clinical

investigation. *Dr. Pardee's* research is concerned with the regulation of the actin cytoskeleton by actin-binding proteins. Regulatory proteins, such as myosin, severin and an actin filament bundling factor, have been isolated and are being analyzed for their roles in cell migration and neoplastic transformation.

The interaction of various cytoplasmic oncoproteins with membrane receptors is the major interest of *Dr. Resh's* laboratory.The laboratory is investigating the association of the myristylated *src* protein with the plasma membrane, an association which is necessary for *src*-mediated neoplastic transformation.Two main areas of research are the identification of the myristyl-src receptor and the enzymology of protein myristylation. *Dr. Robertson's* research involves structural and functional analysis of biologically important RNA molecules. A current focus of interest is the RNA genome of the viroid-like hepatitis delta agent, recently shown to be a ribozyme by Dr. Robertson's laboratory.The focus of *Dr. Rodriguez-Boulan's* laboratory is the regulation of the normal and the transformed epithelial cell phenotype.The roles of protein targeting, the cytoskeleton, and regulatory signals and growth factors are studied using biochemical, immunological, virological and molecular techniques in combination with modern video and electron microscopy procedures. *Dr. Rosen's* research is concerned with the role of activated *src*-related tyrosine protein kinases and the IGF-I receptor in the biology of human colon and breast carcinoma. Current projects include analyses of how *src* and *lck* become activated in colorectal cancer and how the mitogenic signal induced by IGFs in breast cancer is transduced.The work in *Dr. Rothman's* laboratory is focused on intracellular protein sorting. An *in vitro* transport system derived from Golgi stacks has been developed; this system allows a biochemical analysis of protein sorting and the associated protein modifications. Biochemical analysis of one factor (NSF) essential for the transport process is under way. *Dr. Silverstein's* interests concern the events that occur on the surface of platelets and vascular cells during thrombosis and atherosclerosis. His laboratory is pursuing a molecular biological analysis of proteins expressed preferentially on the surface of activated platelets, as well as examining relevant features of cell-cell and cell-matrix adhesion.

Dr. Sonenberg's long-range objective is the molecular description of membrane transduction of peptide hormonal messages after interaction with a specific membrane receptor or other membrane component. *Dr. Staiano-Coico's* research focuses on investigating the regulation of growth and differentiation of epithelial cells.The laboratory employs a number of molecular, biochemical and flow cytometric techniques to characterize the changes which epithelial cell subpopulations undergo during transition to a terminally differentiated state.The main focus of *Dr. Traktman's* research is a molecular genetic analysis of vaccinia virus. Of particular interest are the temporal regulation of gene expression and the coordination of viral DNA replication. A variety of molecular, genetic and biochemical techniques is being employed to identify and characterize the viral genes and enzymes involved in DNA replication, recombination, and the maintenance of DNA topology. *Dr. White's* laboratory studies molecular defects associated with inherited disorders of steroid metabolism, and is elucidating the mechanisms by which these disorders affect growth, sexual differentiation and blood pressure homeostasis. *Dr. Wiedmann's* research is focused on the translocation of proteins across membranes. Identification and analysis of proteins which participate in moving nascent polypeptides across the membrane of the endoplasmic reticulum is of particular interest.The main interest of *Dr. Zakim's* laboratory is solvent-solute interactions in membranes, in which the polymethylene chains are the solvent and proteins or small apolar molecules are the solutes.A major emphasis is on how these non-specific effects regulate the functions of integral membrane proteins.

Recent Publications

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Immunology

Faculty

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Kendall A. Smith
Kurt H. Stenzel
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Osias Stutman
Marc E. Weksler
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Research Activities

The main interests of the Immunology faculty are focused on the complex molecular and cellular mechanisms responsible for the development and regulation of the immune system. Research programs can be grouped into three main areas: (1) immunogenetics of cell surface molecules involved in the differentiation and function of normal and malignant lymphoid cells; (2) cellular immunology of the interactions between cells and their secreted products, and (3) tumor immunology of the transformed tumor cell and its host, aimed at designing possible diagnostic and therapeutic strategies. Research in all three areas involves studies using both animal models and human cells. Immunology is multidisciplinary in its approaches and has generated its own methodology (such as the production of monoclonal antibodies, and the continuous *in vitro* growth and cloning of lymphoid cells), in addition to using the methods of other disciplines, including biochemistry and molecular biology. For example, the analysis of the biological significance of a given lymphoid cell surface antigen is not only studied using classical genetics and in functional assays using monoclonal antibodies, but also by isolating the molecule and defining its structure using biochemical techniques and characterizing its gene with the tools of molecular biology. Thus, the general approach of the research program is to define immunological events at the biological, biochemical and molecular levels.

In the field of tumor immunology, *Dr. Albino's* laboratory is examining the role of specific oncogenes in the pathogenesis of malignant melanoma and renal carcinoma. This includes a comprehensive study of the steps required for the transformation of human melanocytes and proxymal tubule cells. In addition, this laboratory also studies the structure and function of melanoma cell-surface differentiation proteins and their gene sequences.

Dr. Chiorazzi's laboratory is investigating the mechanisms and cellular interactions involved in B lymphocyte activation and differentiation to antibody secreting cells. Studies of selected lymphoid cell-surface receptors and their ligands are integral

components of these analyses. Monoclonal populations of lymphoid cells, derived by either Epstein-Barr virus transformation or somatic cell hybridization, are frequently employed in this approach. Structural and functional studies of antibodies produced in certain autoimmune disorders have provided basic clues to the relationship between normal and disease states. Autoimmune and allergic disorders as well as the chronic lymphoid malignancies are this laboratory's clinical interests.

Dr. Crow is a member of the Cellular Immunology Laboratory at the Hospital for Special Surgery. Two of the collaborative projects she is involved in are: the role of microbial superantigens in T-cell activation, B cell differentiation, and autoimmune diseases; and the investigation of autoantigen-reactive T cells in patients with systemic lupus erythematosus.

The central themes for *Dr. Dupont's* laboratory are the characterization of the genetic composition of the genes of the human major histocompatibility complex (MHC); the investigation of the molecular genetic basis for the expression of these extensive genetic polymorphisms of the MHC-encoded cell surface antigens as detected in the population; and the biological role of MHC gene products in immunoregulation and other biological functions. The laboratory is also involved in investigations in the area of transplantation immunology, particularly in relation to the understanding of mechanisms responsible for graft vs. host disease.

The major focus of the laboratory of *Dr. Elkon* is the investigation of mechanisms of autoimmunity. His current areas of study include: the role of antigen in T-cell activation, molecular defects in lupus T cells, analysis of growth and differentiation of MRL/lpr lymphocyte progenitor and adoptive transfer of lupus cell subsets into SCID mice.

Dr. Friedman is a member of the Cellular Immunology Laboratory at the Hospital for Special Surgery. Two of the collaborative projects he is involved in are: the investigation of the mechanisms involved in T-helper cell-dependent B-cell activation; and the helper T cell-dependent generation of cytolytic T-lymphocyte activity.

For the mouse, the majority of genes encoding lymphocyte antigens are organized in distinct multigene families positioned on several chromosomes. Study of these gene clusters continues to be the major theme of *Dr. Hämmerling's* efforts. The immunogenetics of murine and human lymphoid and hemopoietic cell surface antigens using monoclonal antibodies is another area of Dr. Hämmerling's studies, with special emphasis on their role in T-cell activation.

Dr. Houghton's research program is investigating the expression and regulation of antigens by human tumor cells. Genes coding for these antigens are being identified, sequenced and expressed. The role of differentiation and malignant transformation in the expression of these antigens is an area of active study. Antigens on tumor cells that are potential targets for recognition by the immune system are of particular interest.

The primary investigative interests of *Dr. Kimberly's* laboratory are the study of human Fcγ receptor polymorphisms, the functional capacity of different polymorphic forms and their relationship to the pathogenesis of autoimmune disease. Studies are being conducted in the following areas: Molecular variants of FcγRI; signal transduction of FcγR isoforms; allelic polymorphisms and receptor function; and glycoforms and receptor function.

The molecular genetics of the human major histocompatibility complex or HLA genes is the major area of study of *Dr. Lee's* laboratory. Her goals are to identify and characterize genes and their products that govern the tissue specific expression of class II genes. These studies involve the analysis of defects in expression of mutant cell lines derived from immunodeficiency patients. In addition, the laboratory is investigating regulatory polymorphisms associated with different alleles.

Investigations of the glycoproteins and glycolipids of human tumor cells and normal cells are the focus of research in *Dr. Lloyd's* laboratory. Particular emphasis has been placed on the biochemical identification and characterization of these components.

Dr. Murray has several inter-related research interests. These include (1) macrophage activation for antimicrobial activity, (2) intracellular infections caused by *Toxoplasma gondii* and *Leishmania donovani*, (3) interferon-gamma, and (4) the AIDS T-cell defect.

Dr. Nathan's efforts are aimed at understanding how phagocytic leukocytes kill microbes, tumor cells, and normal host elements at inflammatory sites. Investigations into the biochemical bases of cytotoxicity by macrophages and granulocytes are integrated into a context of cell biology and clinical investigation.

The focus of *Dr. Nikolic-Zugic's* laboratory is on the ontogeny of T cells and their differentiation in the thymus. This laboratory is also investigating the interaction of the major histocompatibility complex (MHC) encoded molecules and the TCR during the positive selection of T cells in the thymus.

Dr. Novogrodsky's research interests include mechanisms of lymphocyte activation, oxidative mitogenesis and effector mechanisms mediated by mononuclear cells and cytokines. Current work involves the mitogenic properties of hemin and its analogs and other iron-containing agents (the ferro-mitogens), and the evaluation of their immune stimulatory and anti-tumor activity.

Dr. Old's research is concerned with the development of two new approaches to cancer therapy: tumor necrosis factor (TNF) and monoclonal antibodies directed against surface determinants on malignant cells. The latter is part of a general effort to analyze the cell surface of human and murine tumors, with the aim to characterize the important surface molecules, mostly with monoclonal antibodies and other serological procedures.

The principal objective of *Dr. O'Reilly's* Bone Marrow Transplantation Program is the development and improvement of transplantation approaches for the treatment of lethal disorders of the blood system through an integrated program of clinical and basic research in immunology, hematology, genetics, and transplantation biology.

Dr. Posnett's laboratory is interested in basic problems of immunology. The approach is primarily molecular. The topics under study include the human T-cell antigen receptor and several lymphocyte membrane molecules that may serve as lymphokine receptors. In the former case he is interested in understanding the process of antigen/MHC recognition by T cells. Studies are focusing on T-cell antigen receptor V gene usage and its relationship with antigen/MHC reactivity. Also of interest are disease associations with the T-cell antigen receptor genes. He is also cloning the genes of several putative lymphokine receptors. These studies are aimed at understanding the function of these membrane activation antigens.

The main objective of *Dr. Rettig's* research is to define the rules and molecular mechanisms by which intrinsic genetic differentiation programs, extrinsic differentiation signals, and malignant transformation are integrated in specific cell types to generate the complex cell-surface patterns seen in human tumors.

Dr. Russo's research is concerned with the role of MHC molecules in regulation of the immune response. Two major areas are under investigation: (1) the dual function of MHC class II molecules in the induction of self-tolerance and in the biology of the autoreactive T-cell network, (2) the relationship between selective loss of MHC class I molecules by tumor cells and tumor progression.

The main interest of the laboratory of *Dr. Salmon* is to examine the structure-function relationships among Fcγ receptors (FcγR) on human phagocytes and their implication for susceptibility to and pathogenesis of systemic lupus erythematosus. Studies are being conducted in structure-function relationships among the alleles of

FcγRIII and FcγII; mechanism for the altered phagocytosis among HLA-DR2 and DR3-positive disease-free subjects and SLE patients; and characterization of the nature of association of HLA class II antigens and the defect in FcγR-mediated function.

Dr. Schwab's research focuses on age-associated changes in the activation signal transduction mechanism via the T-cell receptor CD3 complex and IL-2 receptor.

Dr. Siskind is concerned with factors regulating the immune response. In particular, he is studying (1) the role of idiotype anti-idiotype interactions in determining clonal expression and (2) the role of T cells bearing receptors for the Fc of IgD in regulating the magnitude of the immune response.

Two of *Dr. Smith's* ongoing projects are: focusing on the IL-2-stimulated molecular pathways that promote cell cycle progression; and the other is directed towards understanding the cellular and molecular basis for IL-2-promoted differentiation of naive T cells to memory T cells.

Dr. Stenzel's studies have focused on biochemical mechanisms of lymphocyte activation, transplantation immunology and the role of cell mediated cytotoxicity in the control of cancer growth. The latter studies include both basic and clinical investigation of adoptive immunotherapy in renal adenocarcinoma.

The system being studied in *Dr. Stoeckle's* laboratory is the regulation of pro-inflammatory cytokine genes in fibroblasts in response to interleukin-1 (IL-1).

Dr. Stutman's research is focused in two areas: (1) the ontogeny, maintenance and involution of functional T cells, including T-cell subsets and the role of the thymus proper in such processes, and (2) the immunological components of the tumor-host interaction, especially the production of cytotoxic effector cells which can kill tumor cells by production of tumor necrosis factor (TNF) and other lytic molecules.

Dr. Weksler's research concerns two areas: (1) the biology of autoreactive T lymphocytes and (2) the immunobiology of aging. The former studies are aimed at understanding the development and regulation of the immune system; the latter at understanding the biological processes that lead to the diseases of aging.

Dr. Yang's laboratory is conducting studies of the molecular mechanisms controlling class I MHC gene expression during cellular differentiation and neoplastic transformation, as well as the biological role of class I MHC determinants in tissue transplantation. Another area of study is the activation and differentiation of T lymphocytes and characterization of T-lymphocyte differentiation antigens and their function.

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Molecular Biology

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Research Activities

The faculty of the Graduate Program in Molecular Biology offers graduate research training in a variety of systems on problems related to the replication, transcription, translation and function of genetic information in developing organisms and differentiating cells. The research activities of the faculty can be divided into four broad areas of study: DNA replication and recombination; regulation of RNA synthesis and processing; receptors and their role in cell function and differentiation; and retroviruses, proto-oncogenes, and development.

DNA Replication and Recombination

DNA replication in prokaryotes is under study in the laboratories of *Dr. Marians* and *Dr. O'Donnell*. Dr. Marians focuses on studies of the enzymological mechanisms of DNA replication in *Escherichia coli*, using cell-free systems. The use of *in vitro* DNA replication systems composed of purified replication proteins enables detailed analyses of the interaction of the replication proteins with each other and with the DNA template. The role of topology in DNA replication, as well as the mechanisms of DNA topoisomerases, is also under study in his lab. A detailed examination of the molecular mechanics of DNA replication is also the focus of Dr. O'Donnell's laboratory. The dynamic motions on templates of the multi-protein replicative polymerase of *E.coli* and its interaction with other proteins at the replication fork are under study. Dr. O'Donnell is also investigating the control of replication initiation in Epstein-Barr virus.

Faculty investigating eukaryotic DNA replication employ several different viral systems. *Dr. Berns* uses the life cycle of the human adeno-associated virus AAV2 to model how gene expression and DNA replication are regulated. *Dr. Hurwitz*'s laboratory uses the adeno and SV40 viral DNA replication systems as probes for the

enzymatic mechanisms of cellular DNA replication. The regulation of bovine papilloma virus DNA replication is studied by *Dr. Lusky* using molecular genetics to define and characterize the viral genes required for replication *in vivo* and using biochemical approaches to study BPV DNA replication *in vitro*. The replication of AAV, adenovirus, SV40, and BPV require host cellular proteins; thus these viral systems also allow these investigators to study the endogenous mechanisms for DNA replication in mammalian cells.

Dr. Traktman's laboratory studies the replication of vaccinia virus, a large DNA virus that encodes its own DNA replication machinery. Both biochemical and molecular genetic techniques are employed to define the genes of vaccinia virus that are required for its replication.

The molecular processes controlling the structure, function, and genetic properties of chromosomes are being studied by the laboratories of *Drs. Lustig* and *Hackett*. Using molecular genetics and biochemistry, Dr. Lustig is investigating the mechanisms that have evolved for replicating telomeres, the unique ends of chromosomes required for stability, and the role these sequences play in chromosome segregation and recombination. Dr. Hackett is interested in the structure of the bacterial genome and how it changes over time. His immediate objective is to construct detailed restriction maps of the genomes of several related isolates of *Halobacterium halobium*. Comparisons will reveal how genome structure evolves both normally and in response to selective pressure.

Another key cellular process that occurs on DNA is the exchange of genetic information through the process of recombination. *Dr. Holloman*'s laboratory studies the genes and the enzymes involved in this complicated process. Model studies focus on the mechanism of synapsis and DNA strand exchange.

Regulation of RNA Synthesis and Processing

Many aspects of the regulation of gene transcription and RNA processing are under active investigation by members of the Molecular Biology Program. These include the definition of controlling DNA and RNA sequences, the identification and characterization of the proteins and enzymes involved, and the elucidation of the mechanisms that dictate temporal and spatial patterns of gene expression.

Using genetic and molecular biological techniques, *Dr. Osley* is investigating the basis of the periodic expression of the histone genes in yeast and the connection between chromatin structure and gene transcription.

Research in *Dr. Sheffery*'s laboratory is directed at understanding how proteins and DNA interact to form structures that influence gene transcription, using the mouse globin genes as a model. Particular effort is devoted to understanding tissue-specific gene expression.

In a related effort, the basis of sequence-specific recognition of DNA by proteins is studied by *Dr. Barany* using a combination of molecular biology and biochemistry. One of these proteins, *Taq* ligase, is also used for detecting genetic diseases.

Dr. Falck-Pedersen is characterizing the regulatory elements involved in eukaryotic transcription termination and RNA processing using genetically reconstructed adenovirus as a model vector. Both biochemical and genetic aspects of transcriptional control, with particular emphasis on transcription termination in purified *in vitro* systems, are under study by *Dr. Shuman* using vaccinia virus as a model.

Dr. Dorsett's laboratory is using both genetic and molecular biological techniques to define the *cis*- and *trans*-acting factors that regulate virus-like transposons in *Drosophila.* These transposons are responsible for a number of naturally occurring mutations in *Drosophila* and have been shown to affect the expression of the mutated host genes at the level of transcription.

Dr. Hurwitz's group studies the enzymes and enzymological processes involved in mRNA splicing in human cells.

Receptors and Their Role in Cell Function and Differentiation

Several laboratories are investigating receptors that transmit signals to the interior of the cell after forming a complex with a specific ligand.

In a series of experiments in *Dr. Ravetch*'s laboratory, the molecular genetic analysis of cell surface receptor proteins is being conducted. Receptor modulation, mechanism of signal transduction, and developmental regulation are being studied by isolation and characterization of genes that code for proteins binding immunoglogulins (FC receptors), by studying the interaction of the malaria producing parasite with the erythrocyte, and by characterizing the activated macrophage phenotype.

Dr. Chao's laboratory is studying the mechanism of action of growth factor receptors, such as those interacting with NGF, FGF, EGF, and TNF. In particular, the molecular features that distinguish NGF signaling through its receptor tyrosine kinase are being defined in order to link receptor-mediated events with the steps leading to neuronal differentiation and cell survival.

Using the generation of transgenic mice as the major experimental tool, *Dr. Lacy* is studying the regulation and function of the CD4 and CD8 cell-surface glycoproteins during T-cell maturation in the thymus. CD4 and CD8, respectively, recognize and bind to nonpolymorphic regions on class II and class I major histocompatability complex (MHC) proteins; their interactions with the MHC proteins contribute to the signals transduced by the T-cell receptor during T-cell development and activation.

Retroviruses, Proto-oncogenes, and Development

The research activities of the Molecular Biology faculty in this area are quite diverse and include studies on induced neoplastic diseases, the role of proto-oncogenes in cell and tissue differentiation, embryonic axis formation and the development of the visual system in *Drosophila,* and gene function in the early mouse embryo.

The major objective of *Drs. Hayward*'s and *Zelentz's* laboratories is the elucidation of the molecular basis of the induction of neoplastic disease. Dr. Hayward's laboratory uses avian leukosis viruses as model systems, and is interested in the identification and characterization of oncogenes involved in late stages of tumor progression. Dr. Zelentz's laboratory focuses on the molecular events involved in the genesis and progression of hematolymphoid malignancies. Of particular interest are the mechanisms underlying chromosomal translocation in cancer.

The current research goal in *Dr. Besmer*'s laboratory is to understand the function of the proto-oncogene c-*kit*, a transmembrane receptor kinase. The c-*kit* ligand has been cloned and molecular aspects of c-*kit* mediated signal transmission are being investigated in hematopoietic cell differentiation and development.

Dr. Brown's laboratory is studying a family of genes (*Wnt* genes) that encode intercellular signaling molecules active in embryogenesis and tumorigenesis. A major

focus is the protein product of the proto-oncogene *Wnt*-1 and its mechanism of action in cell culture systems.

Dr Tempst's laboratory studies the regulation, processing and activities of antibacterial peptides, which are major components of the insect immune system. High resolution 2D gel electrophoresis and high sensitivity sequencing techniques are being developed to investigate cellular events at the single protein level.

Drs. DeLotto and *Ballinger* use *Drosophila* as an experimental organism for the study of development and cell determination. Dr. DeLotto studies the mechanisms underlying the formation of the dorsal-ventral axis during embryonic development. Several of the components of the d-v system, *snake*, *easter*, and *gastrulation defective*, are extracellular serine proteases which play a role in a signal transduction cascade. The laboratory is investigating the biochemical interactions of these proteins *in vitro* and *in vivo*. Dr. Ballinger's laboratory is investigating mechanisms of differentiation, pattern formation and behavior in the *Drosophila* visual system with a combination of molecular and genetic techniques. Photo-receptor neurons are the subject of studies focused on a terminal differentiation antigen, and on the mechanism of pattern formation. To investigate the function of complex neural processing networks, behavioral mutations that alter the processing of visual information are under study.

Dr. Lacy's and *Dr. Gudas'* laboratories investigate cell differentiation during mammalian development. Dr. Lacy's group is working on identifying and isolating genes that are required during early post-implantation mouse development by generating insertional mutations in the germ line of transgenic mice. The Gudas laboratory has chosen to employ cultured murine embryonic teratocarcinoma stem cell lines as a model system for molecular studies of embryonic cell differentiation. Of particular interest are the mechanisms by which retinoic acid differentially controls gene expression during the differentiation process and the loss of tumorigenicity of the stem cells.

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Neuroscience

Faculty

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Ellen Townes-Anderson
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Research Activities

Members of the program in Neuroscience use a wide variety of scientific disciplines to study the development and function of the nervous system, including molecular genetics, biochemistry, pharmacology, neuroanatomy, electrophysiology, molecular biology, and behavior. They work at the molecular, cellular, and organismal levels in many animals including rodents, birds, *Drosophila,* reptiles, and *Aplysia,* as well as in humans.The research interests of the program cover the entire range of neuroscience, including the regulation of neural development, neuronal plasticity, control of neurotransmitter synthesis and release, learning, the response of neurons and neural tissue to injury, the regulation of gene expression, endocrine function, vision and other sensory systems, information processing, and behavior. Many members of the program have a special interest in questions that are particularly relevant to human disease, and their research has important implications for topics such as the regulation of pain, neurodegenerative diseases such as Alzheimer's disease and Parkinson's disease, neural tumors, stroke, addiction, and aging.

Dr. Baker studies the factors underlying the determination and maintenance of neuronal phenotype. Using the olfactory system as a model, Dr. Baker focuses her research on neurotransmitter expression during development and aging as well as in response to deafferenting lesions. Immunocytochemical, neurochemical, *in situ* hybridization, molecular biological, and neuronal tracing techniques are utilized in these studies.

Dr. Ballinger's research interests include molecular and genetic studies of the development and function of the *Drosophila* visual system.

Dr. Blasberg's major research interests include the physiology and metabolism of brain tumors and the *in vivo* study of neuroreceptor systems using positron emission tomography (PET). He is developing and coordinating the positron emission tomography program for the Departments of Neurology at Memorial Hospital and New York Hospital in conjunction with the Department of Medical Imaging. He has set up a laboratory for performing quantitative autoradiography and biodistribution studies in small animals to complement the PET program. Active areas of research that are being pursued focus on: a) developing quantitative imaging techniques for measuring the rate of tumor cell proliferation, b) studying the potential of viral therapy for brain tumors, and c) investigating new immunoreactive agents that target unique, tumor-specific epitopes in gliomas; these tumor-specific reagents will be used for new diagnostic and targeted radioimmunotherapy.

Dr. Bovbjerg's major research interest is the interactions between the brain and the immune system in both humans and animal models. He is particularly interested in classically conditioned changes in immune function. Research techniques include a variety of *in-vitro* and *in-vivo* assessments of immune function, as well as a variety of psychobehavioral methodologies. Additional research interests include: the effects of naturalistic and experimental "stress" on immune function in humans; classical conditioning processes in humans; and behavioral effects of immunologic manipulation.

Dr. Caudy is interested in the molecular genetic mechanisms which control neuronal pattern formation during development. He is studying a network of cell determination genes which control the switch between neuronal and non-neuronal cell fates in *Drosophila* embryos. These genes encode a family of DNA-binding transcription factors ("helix-loop-helix" proteins) whose human homologues are proto-oncogenes.

Dr. Chao's laboratory is interested in linking the signal transduction events in the central nervous system with specific transcriptional processes that promote cell differentiation. They have been studying the mechanism of action of NGF, a neurotrophic factor responsible for cell survival and differentiation. They are pursuing the definition of the NGF receptor complex, including the targets of tyrosine kinase phosphorylation, and correlating structural features of the receptor with function using molecular and biochemical approaches and transgenic animals.

Dr. Cooper's research interests include α-keto acid chemistry and biochemistry; pyridoxal 5'-phosphate enzymes; investigations of enzyme mechanisms; design of enzyme inhibitors as drugs; amino acid and ammonia metabolism in normal and disease states; cerebral energy metabolism (with particular emphasis on the malateaspartate shuttle) and its disruption in various disease states; design and use of molecules labeled with short-lived radioisotopes for positron emission tomography of the human tissues and for tracer studies in animals; neurochemical consequences of cerebral ischemia; molecular biology of glutamine transaminase K/cysteine *S*-conjugate β-lyase, ω-amidase in rat kidney; and mitochondrial defects in Alzheimer's disease.

Dr. Duvoisin is interested in studying the molecular basis of retinal function. Molecular cloning has revealed a greater than expected complexity of neurotransmitter receptors and ion channels. The retina, with its well-studied circuitry, is being used to analyze the relationship between molecular diversity and information processing. Ongoing research focuses on glutamate receptors and their role in generating the ON and OFF pathways.

Dr. Fischman is examining gene action within developing muscle cells of the avian embryo. Using retroviral vectors, he is defining the lineages of somitic cells which give rise to limb muscle and altering the expression of selected genes required for normal myogenesis and muscle regeneration.

Dr. Furneaux's laboratory works on the molecular aspects of neurological disease. The focus of these studies is a unique group of antigens which are exclusively expressed in neurons and recognized by the sera of patients with paraneoplastic neurological syndromes, rare disorders in which an anti-tumor immune response is thought to be misdirected against the brain. A number of these antigens have been cloned and characterized, such as HuD, which is a neuronal-specific RNA binding protein and is highly homologous to a *Drosophila* protein (Elav) which controls neuronal cell fate. Another (CD2) is expressed in a subset of mammalian neurons and has features that suggest it functions in the control of neuronal gene expression. Recently we have cloned the target antigen in Lambert Eaton syndrome and have shown that it is the β subunit of the Ca channel complex.

Dr. Gandy's research focuses on Alzheimer's disease, the most common cause of senile dementia. Cerebral deposition of β/A4-amyloid protein is a key feature of the neuropathology of the disease. β/A4-amyloid is derived by proteolysis from a transmembrane precursor, the S/A4-amyloid precursor protein (APP), and mutations in APP segregate with clinical phenotypes of familial Alzheimer's disease. APP is a phosphoprotein, and protein phosphorylation plays a key role in regulating the activity of a standard APP proteolytic pathway which prevents amyloid deposition ("non-amyloidogenic"). In addition, supraphysiologic levels of protein phosphorylation activity appear also to regulate the amyloidogenic pathway of APP proteolysis. By modulating the relative activities of nonamyloidogenic and amyloidogenic pathways for APP proteolysis, protein phosphorylation may regulate the process of cerebral amyloidogenesis. Thus, specific components involved in the regulation of protein phosphorylation represent molecular candidates for etiologic defects and/or targets for potential rational therapies for cerebral β/A4-amyloidoses. Identifying the regulatory components of the APP processing apparatus is the major goal of Dr. Gandy's laboratory.

Dr. Gardner studies how neurons use chemical synaptic transmission to communicate with one another. Neurons in ganglia of the mollusk *Aplysia* are probed by intracellular recording, voltage clamping, patch clamping, and computer-based analysis to yield principles of organization of cell networks. One project focuses on properties of transmitter-activated channels which are altered to produce different postsynaptic currents. A second project combines neurophysiology with artificial intelligence techniques to ask how neuronal biophysics coordinates the activity of neurons in a network.

Dr. Gibbs' research focuses on the neurobiology of motivated behaviors, especially the neuroendocrine mechanisms controlling feeding behavior in animals and the pathophysiology of eating disorders in humans.

Dr. Gibson examines the relation of signal transduction systems (e.g. calcium, PI cascade and cyclic AMP) to oxidative metabolism, neurotransmitters, altered brain function, cell death and gene expression. These interactions are examined in animal models of conditions that alter memory and other mental functions in man (aging, hypoxia/ischemia and thiamine deficiency) as well as in tissues from Alzheimer patients.

Dr. Goldman is interested in neuroplasticity in the adult brain. His research is focused upon the molecular mechanisms subserving neural production, migration and differentiation in a neurogenic region of the adult songbird brain. These cellular events are examined both *in vivo* and *in vitro,* with the aim of determining the regulatory constraints on neurogenesis and neuroblastic migration in the adult CNS.

Dr. Grafstein's primary research interest is in nerve regeneration. At present she is working to characterize the function of a prominent glycoprotein in goldfish brain that has been implicated in neuronal plasticity, including nerve regeneration and learning. Her studies have shown that the protein is primarily localized in non-neural cells, including the meninges, outer wall of blood vessels and leucocytes. Thus this protein may play a role in the interaction between the nervous system and the immune system. Among the techniques used in Dr. Grafstein's laboratory are isotope tracer studies, high resolution autoradiography, immunocytochemistry, electron microscopy and 2-dimensional gel electrophoresis.

Dr. Greenberg focuses on the neuroendocrine mechanisms that control feeding behavior. Specifically, she is investigating neural and hormonal mechanisms mediating satiety induced by ingested fats and the mechanisms underlying increased fat intake in normal and genetically obese animal models.

Dr. Hirsch's research program includes using the new techniques of functional magnetic resonance to understand the signal transmission and network schemes employed by the human brain to code visual and other sensory information. Questions of visual information processing are also addressed by the Vision Lab Group using psychophysical assessments of visual function in conjunction with medical imaging assessments of brain tumors or focal injury.

Dr. Inturrisi studies the molecular basis for the pharmacodynamic effects of opioids and the factors that regulate the endogenous opioid peptide system. Molecular probes are used to define the acute and chronic effects of opioids on the expression of selected genes.

Dr. Job's laboratory is studying molecular genetics of neurotransmitter enzyme genes using multidisciplinary approaches. The studies include structure/function analysis of these genes, gene regulation at transcription level, transgenic mouse models of genetically altered neurotransmission, and molecular mechanisms underlying neuronal degeneration.

Dr. MacLeish's research program focuses primarily on the functional organization of the vertebrate retina. Dissociated neurons from adult amphibian and primate retina are employed to study the electrical properties of identified cells and the physiological properties of synapses formed among the retinal neurons *in vitro*. Voltage-sensitive dyes along with conventional intracellular recording techniques are used to measure electrical activity. A separate area of study is the trans-differentiation of retinal pigment epithelium into neural retina, a process that occurs in adult newts and salamanders. Antibody markers are being generated to describe the regeneration process in more molecular terms and a culture system is being refined to determine the role of soluble factors in regeneration.

Dr. Milner studies the cellular basis for transmitter interactions (1) in the septo-hippocampal pathway important in learning and memory; (2) between opioid neurons in the hippocampal formation involved in seizures; and (3) reticulospinal neurons important in cardiovascular regulation. All three studies utilize either dual labeling immunocytochemistry techniques or immunocytochemical methods combined with tract-tracing techniques at the electron microscopic level of analysis. The major transmitters of interest include catecholamines, acetylcholine, opioids and neuropeptide Y.

Dr. Okamoto researches neuropharmacologic bases of the drug dependence produced by centrally acting drugs in adults and neonates exposed to drugs during their fetal period. Central nervous system depressant drugs, i.e. alcohol, barbiturates and benzodiazapines have been her major interest. Electrophysiologic, neurochemical

and behavioral effects are studied during acute and chronic drug treatment: functional and cellular mechanisms for the tolerance and dependence production are investigated: chronic effects of these drugs are studied on developing synapses and on the maturation of the nervous system.

Dr. Pasternak studies the pharmacology of opioid receptors at the molecular, cellular, and systems level. Molecular approaches include binding studies and affinity labeling of receptors using a series of irreversible opiate agonists and antagonists synthesized in his laboratory. At the cellular level, his group is investigating the second messenger systems mediating opioid actions and potential mechanisms of tolerance. In addition, his laboratory is investigating the role of various opioid receptor subtypes in analgesia. A major question concerns the presence of synergy among brain regions and receptor subtypes. All these studies take advantage of the novel opiates synthesized by his group and are aimed at providing a cohesive view of opioid action.

Dr. Pickel's laboratory is currently examining the synaptic substrates for (1) integration of central autonomic responses to sensory and humoral information, and (2) rewarding and aversive properties of opiates and other drugs of abuse. Of primary interest in these studies are the catecholaminergic and peptidergic neurons located in the brainstem and basal ganglia, respectively. Methods include: electron microscopic immunocytochemistry, *in situ* hybridization, and *in vivo* intracellular physiology.

Dr. Plum, Chairman of the Department of Neurology and Neuroscience, focuses his research efforts on cerebral metabolism in disease states and the identification of cellular-subcellular mechanisms responsible for ischemic cell death.

Dr. Posner is interested in the characterization of "onconeural" antigens shared by the central nervous system and certain tumors and identified by antibodies in the serum of patients with neurological paraneoplastic disorders.

Dr. Reis' research interests are the central neural and neurochemical mechanisms governing control of the autonomic nervous system, cerebral blood flow, and metabolism. His research also includes mechanisms governing the death of brain neurons in response to aging and injury.

Dr. Ruggiero investigates anatomical and neurochemical pathways in brain which maintain normal resting levels of arterial blood pressure; neural substrates of the baroreceptor reflex; pathways underlying the cerebellar regulation of autonomic activities and cerebral blood flow; areas of autonomic representation in cerebral cortex and brainstem reticular formation; adrenaline synthesizing neurons, their pathways in the central nervous system, their role in cardiopulmonary regulation; and afferent (pain) neurotransmission.

Dr. Smith focuses on the behavioral neuroscience of eating and its disorders. Current experiments include the measurement of central monoamines during eating behavior, the role of gut peptides, such as cholecystokinin, in stopping eating, and animal models of eating disorders using genetically obese and sham feeding rats.

Dr. Stokes is interested in neuroendocrine function in affective disease. Measurements of hypothalamic-pituitary-adrenocortical (HPA) function at various levels of this axis are obtained in patients with depression vs. healthy normal controls and patients with other psychiatric diagnoses. Current specific interests include: response of the HPA system to administration of CRF, ACTH, dexamethasone and adrenocortical steroid blockers, pharmacokinetics of dexamethasone, measurement of multiple adrenal steroids, investigation of the relationship between HPA function and biogenic amine and sympathetic nervous system activity. A second area of interest is the investigation of lithium pharmacokinetics and the pharmacology-toxicology of lithium isotopes in animals and humans.

Dr. Townes-Anderson examines the cell biology of retinal neurons. Currently, cells isolated from the adult vertebrate retina are used *in vitro* to address questions concerning synaptic function and plasticity. Membrane recycling at the photoreceptor synapse is being examined with morphological techniques including rapid freezing and electron microscopy. Localization of neurotransmitter receptors is performed on isolated second and third order neurons, and regeneration of functional synapses is being investigated in cultures of adult nerve cells.

Dr. Victor studies visual processing at retinal and cortical levels. Research techniques include single-unit recording, evoked potentials, psychophysics, and mathematical modeling. Other research interests include novel approaches to nonlinear systems analysis and signal processing as applied to neural systems.

Dr. Volpe's laboratory studies learning and memory disorders that are common after ischemic and traumatic brain injury. The laboratory is also studying animal models of learning and memory dysfunction caused by ischemic injury, ablative injury, or toxic insult. Research techniques include the detailed characterization of the behavioral change, quantitative neuroanatomic studies, immunohistochemistry and *in situ* hybridization. Their interest is to determine the extracellular factors governing cell viability and factors regulating tissue-specific gene expression after acute and chronic insults. Understanding the pathological processes involved in these models of brain injury could provide new insights into therapeutic interventions in certain chronic degeration brain diseases.

Dr. Wagner's laboratory is interested in the effects of Nerve Growth Factor, Fibroblast Growth Factor, and other signaling molecules on the development, survival, and differentiation of neural cells. In particular he is interested in the signal transduction pathways that are under the control of these molecules, and the ways they regulate gene expression, morphological differentiation, and enzymatic activity. He is also interested in the role of these molecules in the response to traumatic injury, ischemia, neurodegenerative diseases, and aging.

Dr. Wahlestedt's interests center on neurotransmission and associated intracellular signal transduction. Research projects include (1) molecular cloning of neurotransmitter receptors; (2) studies on novel inositol phosphates involved in Ca^{2+} signaling; and (3) effects of psychostimulant and anti-depressant drugs on brain signaling systems. Clinical collaborations concern hypertension, affective disorders (depression), and drug abuse.

Recent Publications

Baker, H. (with Gorrham, J. D., and Ziff, E. B.), Differential spatial and temporal expression of two type III intermediate filament proteins in olfactory receptor neurons. *Neuron.* 7:485-497, 1991.

Baker, H. (with Farbman, A. I.), Olfactory afferent regulation of the dopamine phenotype in the fetal rat olfactory system. *Neurosci.* 52:115-134, 1993.

Ballinger, D. G., (with Xue, N., and Harshman, K. D.), A *Drosophila* photoreceptor cell-specific protein, calphotin, binds calcium and contains a leucine zipper. *Proc. Natl. Acad. Sci. USA* 90:1536-1540, 1993.

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Pharmacology

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Research Activities

Dr. Bertino is interested in the transfer of drug resistant genes into hematopoietic cells: Viral vectors have been studied as methods of introducing drug resistant genes into mammalian cells in culture and into bone marrow cells. The aim is to produce long-term expression of drug resistant genes in hematopoietic stem cells. The purpose of these studies is to produce drug resistance of marrow stem cells, thus allowing larger doses of the desired drug to be utilized for therapy.

Mechanisms of natural and acquired resistance to folate antagonists and fluoropyrimidines: Human tumor cell lines and fresh human tumor samples (sarcoma, leukemia, colon cancer) are studied to determine mechanisms of resistance to these drugs. Sensitive assays to determine the molecular basis of drug resistance, including gene amplification, gene mutations, and transport and/or defects in drug catabolism have been developed.

Work has been initiated that has as its objective the relationship between oncogene expression and or lack of suppressor gene function on resistance to drugs. An inducible vector system has been developed to express transfected genes for this purpose.

Dr. Blanck's research interests include the characterization of the effects of anesthetics on intracellular calcium distribution in cardiac and neuronal cells. These studies are designed to further the understanding of how volatile anesthetics work to produce general anesthesia, their protective effects during ischemia, and their depressive effects on cardiac contractility. These varied effects appear to share a common mechanism of action, at least in part, that being the alteration of calcium ion availability and fluxes.

These changes are being studied by examining several calcium sensitive sites in cardiac and neuronal cells. Plasma membrane calcium channel density is characterized by measuring the number and affinity of drug binding sites in the presence of volatile anesthetics. Studies are underway to characterize the functional properties of single

calcium ion channels which have been incorporated into artificial lipid bilayer membranes.

Dr. Buck's interests focus on the structural and functional properties of small lipophilic intracellular signal molecules. Recent findings in several laboratories have demonstrated the potential of this class of molecules to serve as ligands for nuclear receptors. Well-studied examples are steroids and retinoic acids that have an important function in transcriptional regulation via the steroid receptor superfamily.

During recent years Dr. Buck characterized in collaboration with Dr. Hämmerling two new intracellular messenger molecules, 14-hydroxy-*retro*-retinol (14-HRR) and anhydroretinol (AR). Lymphocyte activation and proliferation is critically dependent on an external source of vitamin A (retinol). After activation, lymphocytes produce 14-HRR from retinol. If 14-HRR production is blocked by AR, a physiologically occurring competitive 14-HRR antagonist, resting T cells cannot be activated and cycling cells die in hours. First data show that the intracellular pathway in T lymphocytes is distinct from the intracellular pathway which is inducing the IL-2 receptor and IL-2 production.

The laboratory is trying to characterize in more detail the regulation and the biochemical pathway of 14-HRR/AR production and metabolism. Of utmost importance is the purification and cloning of intracellular 14-HRR binding proteins/receptors.

Dr. Chan is interested in the functions and interactions of prostaglandins and neurohypophysial peptides in the kidney and the uterus. Current research covers investigative studies from subcellular levels to the whole organism. Certain analogs of oxytocin and vasopressin have been found to stimulate urinary sodium and water excretion. This renal effect of the peptide appears to be mediated by renal prostaglandin release. The biochemical mechanisms of this peptide-induced prostaglandin release are the principal concerns of this research. Also studied are the renal activities of peptide analogs specifically synthesized for the project with the aim to discover specific prostaglandin-releasing and/or anti-vasopressin (anti-ADH) peptides that may be useful for the treatment of renal hypertension.

In the uterus, the roles of prostaglandins and oxytocin in the regulation of uterine contractions and termination of pregnancy are being investigated. This research seeks an understanding of the mechanism of initiation of labor, especially relating to preterm labor. Oxytocin-receptor and gap-junction formations in myometrial cells are important biochemical and morphological markers in the initiation of labor. Accordingly, effects of prostaglandins and oxytocin on the density of oxytocin-receptors and on the formation of gap-junctions in myometrial cells are studied. Highly potent oxytocin antagonists have been synthesized for this project and their application in the prevention of preterm labor in the pregnant rat model will be investigated. Also studied are the physiological roles of ovarian oxytocin and uterine prostaglandins in the function of the corpus luteum, as well as the potential of intervention of this ovarian-utero axis in the regulation of fertility or as causal factor in abortion.

Dr. Chou's research activity includes three areas: 1) developmental therapeutics of new antitumor and antiviral agents using synthetic compounds and plant products; 2) biochemical studies on selected compounds at molecular level with the aims of elucidating mechanism of action, selectivity of effect, or the development of drug resistance and cross-resistance, and 3) theoretical biology of deriving generalized equations based on the principle of mass-action law for dose-effect analysis, receptor topological analysis, and the quantitation of multiple drug interactions in terms of synergism and antagonism. In the first area, preclinical pharmacological studies have been conducted on acridine alkaloids such as glyfoline and synthetic acridines as

anticancer agents, and on 3'-fluro-3'-deoxythymidine (FLT) as an anti-AIDS agent. The latter has entered clinical trials. In the second area, DNA intercalators, such as chrysophanol and acridine derivatives have been studied, as inhibitors of DNA topoisomerase type II. Topoisomerase II mediated-drug induced DNA cleavages and the inhibition of topoisomerase were examined by measuring the relaxation of supercoiled DNA, decatenation of kinetoplast DNA, and the stabilization of the cleavable complex. Monofunctional and/or bifunctional chloroethyl alkylating groups have been added to some of these molecules for active site and binding site studies. In the third area, the median-effect equation and the multiple drug-effect equation for isobologram and FA-CI plots have been derived and computer software for IBM-pc microcomputers have been developed for automated data analysis. The method has been applied in various drug combination studies for anticancer agents, antiviral agents (anti-HIV, anti-HSV, etc.) and for immunosuppressants in organ transplantation.

Dr. Felsen's laboratory is interested in the role of inflammatory mediators or cytokines (including tumor necrosis factor, interleukins, PAF and arachidonic acid metabolites) in the genito-urinary tract. The role of these compounds both *in vitro* and *in vivo* is studied using a variety of techniques. In obstructive uropathy, renal function is assessed through measurement of renal blood flow, glomerular filtration rate, sodium, potassium, and water excretion and other parameters. *In vitro,* cell culture and molecular biological techniques are used to assess renal mediator synthesis by various elements of the genito-urinary tract. In interstitial cystitis (a chronic bladder disease), patient urine and tissue samples are examined for inflammatory mediators in an attempt to both better define this disease and to uncover new treatments for it. Additional studies in the prostate are involved with determining the role of newly described imidazoline receptors and inflammatory mediators in prostate growth and physiology.

Dr. Golde investigates the regulation of normal and neoplastic blood cell formation and the humoral mechanisms involved in modulating mature blood cell function. The biologic basis for the use of colony-stimulating factors (CSFs), interleukins, and certain cytokines is studied at the level of receptor interaction, intracellular signaling mechanisms, and transcriptional activation. The receptor for granulocyte-macrophage CSF (GM-CSF) is a focus of research with an emphasis on the function of soluble alpha subunits which arise by alternative splicing and a delineation of the early events in signal transduction. Dr. Golde has found that an important intermediary signaling pathway in GM-CSF action is enzymatic activation and phosphorylation of the microtuble-associated protein (MAP) kinases. Cytokines and CSFs are also investigated with regard to activation of HIV proviral transcription in model systems using granulocytic, monocytic, and T-cell lines. Mature blood cell function is studied in terms of granulocyte, eosinophil, and monocyte-macrophage function in host defense, analyzing phagocytosis, microbial killing, antibody-mediated and antibody-independent cytotoxicity, and the transport of small molecules such as ascorbate.

The effect of growth hormone, insulin, and insulin-like growth factors is investigated with regard to their interaction with hematopoietic cells, particularly T lymphocytes. Unique virally transformed T-lymphocyte cell lines from patients with genetic abnormalities in responsiveness to insulin, growth hormone, and insulin growth factor-1 (IGF-1) are used in the laboratory to elucidate the cellular pharmacology of these hormones. Particular emphasis is placed on mechanisms of genetic and acquired insulin resistance.

The final area of investigation in the laboratory involves gene therapy. Gene therapy strategies being evaluated include cytokine gene therapy as a strategy for tumor cell immunization. An interleukin-2 (IL-2) gene therapy protocol in melanoma will enter

clinical trial this year. Other gene therapy strategies being investigated include suicide gene therapy, antisense technology, and gene replacement therapy as it relates to cancer.

Dr. Gross' research focuses on nitric oxide, a newly discovered signaling molecule whose function is just beginning to be elucidated. Principal among the known actions of nitric oxide is its key role in vascular homeostasis and blood pressure regulation, its mediation of cytotoxic and cytostatic effects of certain cells of the immune system, and its function as a chemical transmitter/second messenger in the brain. Deficient production of nitric oxide (also known as endothelium-derived relaxing factor; EDRF) by the vascular endothelium has been implicated in hypertension, atherosclerosis and diabetes. On the other hand, overproduction of nitric oxide may be responsible for the hypotension which occurs during bacterial sepsis and in response to the chemotherapeutic use of cytokines. The emphasis of Dr. Gross' research is to reveal biochemical mechanism(s) of nitric oxide synthesis, regulation and actions in physiology and disease.

The laboratory of *Dr. Gudas* has several long-term research aims. One major goal is to learn about the regulation of gene expression during mammalian cell differentiation, while another is to understand the mechanism by which vitamin A and its derivatives (retinoids) control both cellular differentiation and cellular proliferation. Retinoids exert effects on cell differentiation, pattern formation in development, limb regeneration, and the inhibition of the process of tumor formation. As a model differentiation system, the retinoic acid induced differentiation of murine teratocarcinoma stem cells is being studied; these stem cells are similar in many respects to the pluripotent inner cell mass cells of the mouse blastocyst. The teratocarcinoma stem cells differentiate into an epithelial cell type called parietal endoderm when they are treated with retinoic acid. A number of genes which are expressed at different times during this differentiation process have been cloned. Currently the structures of these genes are being determined, including the sequences of their promoters, in order to understand how their expression is regulated during differentiation. The actions of the nuclear receptors for retinoic acid, retinoic acid receptors α, β and γ, are being elucidated, as is the mechanism by which cyclic AMP can enhance the action of retinoids in this system. Finally, since the teratocarcinoma stem cells resemble pluripotent cells of the early mouse embryo, the expression of the teratocarcinoma differentiation related genes in early mouse embryos and in early *Xenopus* embryos are being analyzed.

Dr. Hemmings is interested in the role of protein phosphorylation as a target for the effects of general anesthetics on synaptic transmission in the central nervous system. Specific processes under study that are affected by general anesthetics and also regulated by protein phosphorylation include excitatory neurotransmitter release, excitatory neurotransmitter receptor function and inhibitory neurotransmitter receptor function. Experiments to probe the presynaptic effects of anesthetics employ a functional subcellular model of the synapse (synaptosomes), as well as purified components of the major presynaptic phosphorylation systems. The effects of various general anesthetics on depolarization- or secretagogue-induced neurotransmitter release and on changes in the phosphorylation of specific presynaptic proteins involved in the control of neurotransmitter release will be studied in synaptosomes. The effects of anesthetics on the activities of purified protein kinases, protein phosphatases, and on the phosphorylation and dephosphorylation of purified synaptic proteins by their appropriate purified protein kinases and protein phosphatases are also being studied. Experiments to probe the postsynaptic effects of anesthetics will employ purified neurotransmitter receptors.

A second line of research focuses on the characterization of neuronal protein phosphatases, mechanisms involved in the regulation of their activity, and their role in the regulation of neuronal function. This project involves the application of biochemical and immunological methods to the identification of neuronal phosphatases and their regulators. The role of protein phosphatases in the control synaptic function will be examined using synaptosomes and cultured neuronal cells.

Dr. Inturrisi's research activities are directed toward understanding the biochemical basis of the pharmacodynamic effects of opioids. In laboratory animals studies utilizing molecular probes are aimed at defining the factors that regulate opioid peptide gene expression, biosynthesis and release so as to establish the relationships between treatments that alter opioid peptides and their mRNAs and the functions (e.g., analgesia) of the endogenous opioid peptides. Other studies are examining the links between opioid tolerance and gene expression in selected loci of the CNS. Clinical studies are aimed at developing pharmacokinetic-pharmacodynamic models from patient data that can be used to improve analgesic therapy and provide insight into the quantitative aspects of the development of tolerance to opioids in these patients. The ultimate goal of these studies is a more precise definition of the interrelationship between the exogenous and endogenous pain modulating systems.

Immune hypersensitivity reactions are often associated with severe cardiovascular dysfunction. The long-term goal of *Dr. Levi's* research has been to provide an understanding of the immunopharmacologic mechanisms responsible for the epidemiologically demonstrated association between IgE serum levels and cardiovascular disease.

His laboratory is presently characterizing a recently discovered endothelial dysfunction. Following immediate hypersensitivity reactions, arteries become grossly defective in their response to endothelium-dependent vasodilators and hyperresponsive to vasoconstrictors. The laboratory is therefore assessing the involvement of endothelium-derived nitric oxide (NO) in these reactions in various vessels, coronary included.

Histamine, released by many common non-immunologic stimuli and in myocardial ischemia, is predominantly a vasodilator, but becomes a potent local constrictor at coronary vessel sites affected by atherosclerosis. New tools are now available to assess the biology of NO. Thus the laboratory is determining NO release from the heart, its contribution to histamine's effects on the coronary vessels, and its role in the vasodilatation of the coronaries in response to isolemic events, both in normal and atherosclerotic animals. Because histamine is released in myocardial ischemia, it is conceivable that dysfunctions of the NO system could precipitate histamine-induced coronary spasm leading to myocardial infarction, arrhythmias, and sudden cardiac death.

Dr. Mendelsohn's laboratory is studying the epidermal growth factor (EGF) receptor from a number of points of view. (1) Exogenous and endogenous agents that control autophosphorylation of the EGF receptor are being investigated. These include SGF-α and TGF-α, as well as regulators of protein kinase C, activated receptors for other growth factors, and phosphatases. (2) The interactions between endogenous growth factors (autocrine loops) and other agents that promote or inhibit cell proliferation, including TGF-β and the interferons are being explored. (3) The laboratory has produced anti-EGF receptor monoclonal antibodies that inhibit EGF and TGF-α binding and block receptor activation. These are utilized in the above biologic experiments, and preclinical studies and clinical trials in patients are being carried out, exploring the capacity of antireceptor antibodies to act as antitumor agents. Conjugates of antireceptor antibodies with cytotoxic agents and radionuclides are under investigation in human tumor xenograft model systems.

Dr. Okamoto studies the neuropharmacologic bases of the drug dependence produced by centrally acting drugs in adults and neonates exposed to drugs during their fetal period. Central nervous depressant drugs, i.e. alcohol, barbiturates and benzodiazepines have been her major interest.

Electrophysiologic, neurochemical and behavioral effects are studied during acute and chronic drug treatment: functional and cellular mechanisms for the tolerance and dependence production are investigated: chronic effects of these drugs are studied on developing synapses and on the maturation of the nervous system.

Dr. Pasternak studies the pharmacology of opioid receptors at the molecular, cellular and systems level. Molecular approaches include binding studies and affinity labeling of receptors using a series of irreversible opiate agonists and antagonists synthesized in his laboratory. At the cellular level, his group is investigating the second messenger systems mediating opioid actions and potential mechanisms of tolerance. In addition, his laboratory is investigating the role of various opioid receptor subtypes in analgesia. A major question concerns the presence of synergy among brain regions and receptor subtypes. All these studies take advantage of the novel opiates synthesized by his group and are aimed at providing a cohesive view of opioid action.

Dr. Prochaska's major research interests are geared toward the design and implementation of pharmacological strategies for the prevention of human cancer. Although the carcinogenic process can be disrupted at several points, many recognized anticarcinogens share in common the ability to induce Phase II detoxication enzymes. "Anticarcinogenic enzyme inducers" are present in the human diet, and may play an important role in modulating cancer risk.The laboratory is attempting to elucidate the molecular mechanisms for Phase II enzyme induction so that more potent and less toxic inducers can be identified. Moreover, we are examining the role of these compounds in diseases that increase cancer risk, with the goal that appropriate patient populations can be identified for chemoprevention trials.

Dr. Reidenberg pursues a fundamental question in clinical pharmacology, "Why do different people react differently to the same dose of the same medicine?" His program in clinical pharmacology addresses the question in several different ways. Currently, he is studying the clinical pharmacology of gossypol and other bioflavonoids.This is related to development of gossypol as a male oral contraceptive and the problem of hypokalemia in some men taking this drug. A clinical trial of high dose gossypol in patients with advanced cancer has produced a response in 3 of 18 evaluable patients. Studies of the mechanism of action of gossypol are ongoing to try to develop drugs that improve on gossypol's action on cancer and for fertility regulation.

Dr. Rifkind's interest in environmental toxicology has led to the investigation of the biochemical mechanisms of polychlorinated biphenyl (PCB) and dioxin toxicity. These compounds bind to a cytosolic receptor (Ah receptor) which controls the expression of a group of gene products including specific isozymes of cytochrome P-450. Dr. Rifkind's laboratory is studying the relationship of cytochrome P-450 to the diverse toxic manifestations of PCB and dioxins.These include weight loss, thymic involution, tumor promotion, and cardiac toxicity. Her laboratory recently discovered that the cytochrome P-450 induced by toxic PCBs and dioxins increases the metabolism of the endogenous membrane fatty acid, arachidonic acid, to epoxides and monohydroxylated products.These arachidonic acid metabolites have biologic activities consistent with involvement in PCB and dioxin toxicity. Current studies focus on (1) the role of arachidonic acid metabolism in PCB and dioxin toxicity and (2) the effects of dioxin induced changes in arachidonic acid metabolism on signal transduction pathways in heart and liver.

Dr. Roepe's research is focused on obtaining a molecular-level understanding of the structure and function of adenosine triphosphate (ATP)-coupled active transport systems, particularly multidrug resistance proteins (P-glycoproteins, or MDR proteins), which are involved in making tumor cells resistant to chemotherapeutics. In this effort the laboratory utilizes the tools of molecular biology, biochemistry and biophysics. Biophysical approaches include both solution and single cell-based fluorescence studies of transport phenomena. In particular, single-cell photometry methods have recently been used to analyse the transport of various ions in multidrug resistant tumor cells. Another major activity of the laboratory is recombinant DNA-based overexpression and subsequent reconstitution of membrane proteins, for more biochemical studies. Other molecular biological studies include site-directed mutagenesis to define substrate binding sites, gene fusion studies to assess membrane protein topology and target gene disruption, and studies on the mechanisms of gene amplification.

Dr. Scheinberg evaluates immunologic approaches to the study and therapy of human leukemia and lymphoma. The overall goals of the Hematopoietic Cancer Immunochemistry Laboratory are to identify and understand the functions of specific cell surface molecules on normal and neoplastic hematopoietic cells and, if possible, to use these molecules as targets for immunotherapy. This includes identification of cell-surface targets, development of new immunotherapeutic agents, and phase 1 study of these new agents in patients at Memorial Hospital with an emphasis on the use of monoclonal antibodies (mAb) as pharmacologic agents for therapy of leukemia and lymphoma. MAb may be used pharmacologically as carriers of potent toxins or isotopes specifically to tumor cells, as direct mediators of immune cell killing via complement or as regulators of growth via cell surface receptors. Projects focus on applying these approaches to the therapy of human leukemia and lymphomas; one project seeks to identify novel targets for immunotherapeutics. Currently being studied are: (1) M195, an mAb to CD33, which is restricted to early myeloid progenitors and acute myeloid leukemia (AML) cells; this mAb is active in the treatment of AML; (2) JD 118, a cytotoxic mAb, reactive with a B cell activation antigen and OKB7 mAb reactive with B cell lymphomas and leukemias; (3) the role of glycosphingolipids in B cell differentiation and neoplasia.

Dr. Scotto's laboratory is interested in the role that transcriptional and post-transcriptional regulation play in the development and maintenance of the multidrug resistance (MDR) phenotype. In multidrug resistance, which is observed both clinically and in tissue culture, cells that are challenged with vinca alkaloids, actinomycin D or anthracycline antineoplastic agents develop resistance not only to the selective agent but also to a broad spectrum of functionally and structurally unrelated compounds. This resistance is primarily mediated by the overexpression of a plasma membrane protein, P-glycoprotein, which facilitates drug efflux. The regulation of the P-glycoprotein genes in human, hamster and mouse is being investigated with respect to 1) the DNA (cis) elements and protein (trans) factors involved in the transcription of this gene in drug-resistant cells; 2) the modulation of P-glycoprotein gene expression during the cell cycle and differentiation of secretory cells; 3) the contribution of post-transcriptional and post-translational modifications to the MDR phenotype.

Dr. Sirotnak's research focuses on (1) molecular targets and other cellular biochemical determinants important to selective antitumor action of various categories of cytotoxic antimetabolites; (2) cytoplasmic membrane transport of pharmacologic agents; (3) molecular mechanisms of acquired resistance of tumor cells to antineoplastic agents; (4) the regulation of folate and nucleoside transporter gene expression; and (5) the regulation of antifolate embolism at the level of q-gene expression

Folates play a crucial role in the biosynthesis of macromolecules. Access of tumor cells to exogenous plasma folate is made possible by the existence in the cytoplasmic membrane of a specific high-affinity transport system. Using c-DNA probes, the genetic regulation and molecular biology of this system are now being examined in models which constitutively overproduce or underproduce the transport protein and during induction of tumor cells to terminal maturation.

Folate and nucleoside analogs effectively accumulate in tumor cells via plasma membrane systems normally transporting natural folates and nucleosides. To understand the selective antitumor action of folate and nucleoside analogs, studies are being conducted of the properties and multiplicity of their cellular membrane transport, their interaction with enzymic and macromolecular targets, their intracellular metabolic disposition and their pharmacokinetic behavior. Mechanisms of acquired resistance in tumor cells of these antimetabolites and other cytoxic agents at the level of their cellular membrane transport metabolic disposition and enzymic targets and regulation of their gene expression are studied.

Dr. Szeto's research focuses on the development of novel opioid drugs as obstetrical analgesics. Opiate drugs, such as morphine and meperidine, are widely used for pain relief during labor and delivery. Their use, however, is associated with a variety of side effects in the mother, including sedation, hypotension and respiratory depression. In addition, these drugs have been shown to decrease fetal heart rate variability, and cause respiratory depression and abnormal behavior in the newborn. Opiate drugs may adversely affect the fetus directly as a result of placental drug transfer, and/or indirectly by altering the delivery of oxygen and substrates to the fetus. Two different approaches are being used in the design of opioid drugs with fewer side effects on the fetus and newborn. One approach is to minimize the extent of placental transfer by using opioid peptide analogs rather than the conventional alkaloids. The second approach is to take advantage of the multiple classes of opioid receptors, and try to separate analgesia from the other effects of the opioids. The overall research effort involves the rational design and synthesis of novel opioid peptides with high selectivity for the μ and the δ receptors, and with varying degrees of lipophilicity; determination of the pharmacokinetics of these peptide analogs in the mother and fetus; and the determination of the effects of these peptide analogs on hemodynamic, respiratory, metabolic and neuroendocrine control in the mother and fetus.

Dr. Watanabe has a broad interest in various facets of organic chemistry and biochemistry, especially in the development of new chemical reactions and their application to the design of novel molecules that exhibit anticancer and/or antiviral activity, or that are useful in elucidating enzyme reaction mechanisms. Many analogues of nucleic acid components and folic acid have been designed and synthesized using new chemistry developed in Dr. Watanabe's laboratory. Some of these compounds underwent clinical studies. Novel intercalating agents that bear covalent bond-forming capability have been synthesized, some of which showed potent activity against topoisomerases and many cancer cell lines.

More recently, Dr. Watanabe's group synthesized oligonucleotides containing modified nucleosides and their physico-chemical and biochemical properties studied. The basic knowledge obtained with the synthetic oligonucleotides will be applied in the development of antisense and antigene strategies for development of more selective anticancer and antiviral drugs.

Recent Publications

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Physiology and Biophysics

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Research Activities

The Faculty of the Graduate Program in Physiology and Biophysics offers graduate research training in a wide variety of areas related to understanding function at the molecular, cellular, organ, and system level. The research interests of the faculty are concentrated among the following areas: the structure, function, and regulation of ion channels and other integral membrane transport proteins; intracellular electrolyte homeostasis and renal function, mechanisms of hormone action, receptor turnover, and gene regulation; cardiovascular physiology, nervous and visual system function, development, and regeneration; integrated models of epithelial and renal function; and radiation biology.

Dr. Andersen is interested in the molecular mechanisms that govern membrane protein structure and function. This general problem is addressed in experiments on membrane-spanning channels. At present, the following issues are under active investigation: how do the primary amino sequences encode the conformation of membrane-spanning channels; how do individual amino acid residue substitutions modulate function; how can individual channels function in several distinct modes; and what are the mechanisms by which the host bilayer can modulate channel function? The primary techniques used in the lab include: single-channel and other electrophysiological measurements, kinetic analysis, and simulations.

Dr. Duch's laboratory investigates the molecular interactions which define and control the functions of ion channels. This work reconstitutes purified and unpurified sodium channels from the electric organ of the electric eel and the human brain into planar lipid bilayers in order to probe the molecular interactions between the protein and non-protein (carbohydrate and lipid) domains of these channels. These interactions may play important roles in regulating channel function. In a related project, the mechanisms by which anesthetics modify ion channel function are being examined on a single channel level. These experiments, also conducted with sodium channels in planar lipid bilayers, are designed to probe the intermolecular interactions which define the anesthetic response.

Dr. Gardner's laboratory studies how neurons use chemical synaptic transmission to communicate with one another, and how networks of neurons process information.

Recent discoveries suggest that postsynaptic neurons can specify synaptic strength by controlling the amount of neurotransmitter that presynaptic cells release upon them. Other findings show that synaptic strengths of invertebrate neurons resemble those in theoretical models.Techniques used by Dr. Gardner include electrophysiological voltage- and patch-clamping, computer data acquisition and analysis, and comparison of network behavior of biological and computer-simulated neural networks.

Dr. Gershengorn's laboratory focuses on delineation of the mechanism of binding, activation and regulation of the G protein-coupled receptors for thyrotropin-releasing hormone (TRH) and calcitonin. Another interest of this laboratory is the use of adenovirus vectors to specifically target cells for gene transfer.

Dr. Grafstein's primary research interest is in nerve regeneration. At present, she is working to characterize the function of a prominent glycoprotein in goldfish brain that has been implicated in neuronal plasticity, including nerve regeneration and learning. Her studies have shown that the protein is primarily localized in non-neuronal cells, including the meninges, outer wall of blood vessels and leucocytes. Thus this protein may play a role in the interaction between the nervous system and the immune system. Among the techniques used in Dr. Grafstein's laboratory are isotope tracer studies, high-resolution autoradiography, immunocytochemistry, electron microscopy and 2-dimensional gel electrophoresis.

Dr. Koutcher's research focuses on *in vivo* applications of nuclear magnetic resonance (NMR) to the study of hematologic and neoplastic diseases.These studies are performed in animal tumor models (mice), cell culture systems, and in patients.The focus of much of the work is to determine whether tumor metabolism, as monitored by *in vivo* NMR spectroscopy, can be used to 1) determine tumor sensitivity to antineoplastic therapy, or 2) to enhance treatment by optimizing the choice or timing of therapy based on changes in tumor metabolism. More recently ^{1}H volume localized spectroscopy has been used for the study of bone marrow in patients with hematologic diseases.These studies are being expanded to cell models.

Dr. Li's experiments have shown that of the many heat shock proteins (hsp's) preferentially synthesized after a heat shock, the concentration of hsp70 appears to correlate best with heat resistance, either permanent or transient.The long-term goal of Dr. Li's research project is to establish the molecular basis related to the role that hsp 70 plays in modulating cellular responses to heat and drugs or other environmental stresses. Current research emphasis is placed on the following: (1)To develop and characterize a model system to study the physiological functions, cellular targets and biochemical properties of hsp70 by mutagenesis of the cloned human hsp70 gene. Using the system developed, Dr. Li plans to study the structural domains and functions of hsp70. Specifically, she will address questions on what mutations in hsp70 gene will alter its biochemical properties, its cellular targets and/or physiological function(s). (2)To study of the role of hsp70 in protecting macromolecules or protein complexes from heat-induced denaturation (inactivation or insolubilization), using *in vivo* and *in vitro* model system; to investigate the structural domain of hsp70 responsible for this role. (3)To develop a practical assay using hsp70 as a means to predict and monitor heat resistance and thermotolerance in various cell lines and tissues. (4)The study of the interrelationships between heat response, thermotolerance, drug resistance, and heat-drug interaction.

Dr. Ling is interested in the biological effects of radiation pertaining to radiation carcinogenesis and to the application of radiation for cancer radiotherapy. At present, four areas of research are conducted in his laboratory: (l) physical dosimetry as it

pertains to clinical radiation oncology, particularly brachytherapy; (2) radiobiology of low energy and short-lived isotopes; (3) radiation-induced oncogenic events in carcinogenesis; and (4) the influence of oncogene expression on cellular radiosensitivity.

Dr. Lipkin's studies have been directed to measurements of abnormal stages of cell development that are associated with increased susceptibility to cancer. They include studies of abnormally proliferating and differentiating cells, and gene structure and expression during the evolution of neoplasms. The findings are applied to test mechanisms of action and potential utility of chemopreventive agents both in rodent models and in human subjects. The effects of specific nutritional modifications on colonic epithelial cell proliferation and differentiation are analyzed to guide the development of new classes of chemopreventive compounds, and to test their efficacy.

Dr. Maack's studies are directed to the elucidation of the physiology of cardiovascular hormones and their receptors as well as the organ and cellular processing of peptide hormones and their receptors. In the past few years, the laboratory has been dedicated to the study of a novel polypeptide hormone, atrial natriuretic factor (ANF). Studies in the laboratory elucidated the structure of ANF as well as the main functional actions of the hormone on the kidney and cardiovascular system. More recently, the laboratory discovered that a main class of ANF receptors in kidney and vasculature is involved in the removal of ANF from the circulation and plasma homeostasis of the hormone. Studies are presently under way on the cellular physiology of ANF binding, internalization, lysosomal hydrolysis and on the recycling of ANF receptors in cultured cells. The techniques used in Dr. Maack's laboratory include studies in intact anesthetized and conscious rats, isolated perfused rat kidney, cell culture, receptor-hormone interactions, and general biochemical and physiological techniques.

Dr. MacLeish's research program focuses primarily on the functional organization of the vertebate retina. Dissociated neurons from adult amphibian and prime retinae are employed to study the electrical properties of identified cells and the physiological properties of synapses formed among the retinal neurons *in vitro*. Voltage-sensitive dyes along with conventional intracellular recording techniques are used to measure electrical activity. A separate area of study is the trans-differentiation of retinal pigment epithelium into neural retina, a process that occurs in adult newts and salamanders. Antibody markers are being generated to describe the regeneration process in more molecular terms and a culture system is being refined to determine the role of soluble factors in regeneration.

Dr. Palmer's research focuses on the mechanism of transepithelial Na^+ and K^+ transport by tight epithelia, and the control of this process by hormones. The major effort is to define the nature of the channels responsible for the movement of these ions across the luminal cell membrane of epithelia, and to identify the intracellular agents which affect the function of the channels. The experimental model being investigated in most detail is the rat cortical collecting tubule. Information about the functional properties of the channels and their regulation is obtained using electrophysiological approaches, especially single-channel and whole-cell current analysis using patch-clamp techniques. The molecular properties of the channels are also being investigated. A renal K^+ channel belonging to a new channel family was recently cloned and sequenced using expression cloning in *Xenopus* oocytes. The biophysical properties of this channel, as well as its distribution and function within the kidney, are currently being studied.

Dr. Pickering's main area of research is concerned with development of improved methods for the noninvasive measurement of blood pressure. First, he is using ambula-

tory monitoring techniques to learn more about the causes of blood pressure variability in normal and hypertensive subjects. This work has shown that most of the observed circadian rhythm of blood pressure can be accounted for by changes of activity and that blood pressure variability is an independent risk factor for coronary heart disease. Second, with Dr. Seymour Blank, he is analyzing the causes and origins of Korotkoff sounds with a view to the development of a new technique for blood pressure measurement.

Dr. Rayson's research activities center on the investigation of the regulation of synthesis of the Na^+/K^+-ATPase enzyme (the Na^+ pump), a pivotal enzyme in the regulation of intracellular electrolyte levels. In addition, the regulation of the synthesis of renin, a principal determinant of blood pressure and total body fluid and electrolyte balance is under investigation. Both projects involve analysis of a range of steps within the protein synthetic pathway, employing molecular biological technology.

Dr. Sackin's research interests have focused on the electrophysiology of renal epithelia. Recent work has utilized the patch clamp technique to study single channel and whole cell currents in the proximal tubule and collecting duct of the kidney, with particular emphasis on the role of stretch-activated ion channels. These mechanosensitive channels alter their electrical gating properties as a function of membrane tension. They can act as micro-transducers that convert pressure and osmotic information into electrical currents. This may be important for both volume regulation and electrolyte homeostasis. Experiments are also in progress using patch-clamp techniques to study renal potassium channels expressed in *Xenopus* oocytes.

Dr. Sealey and her colleagues are addressing the question of the coordination of the roles of renin gene expression in the kidney and reproductive organs. They investigate the mechanism whereby tissues that abundantly express the renin gene avoid interference with the circulating renin system in which very low levels of plasma renin are vital for maintenance of blood pressure. Dr. Sealey has evidence that the functions of tissue and circulating systems are separated by the actions of two different renins. Active renin continuously forms angiotensin in the circulation. Prorenin, previously thought to function primarily as biosynthetic precursor of renin, has been shown to have its own renin-like activity. Current research focuses on the idea that prorenin catalyzes tissue angiotensin formation when it binds to a receptor. This allows separation of the different effects of circulating and tissue renin systems. This work may lead to the development of specific pharmacologic agents enabling selective blockade of renin system at different target sites.

Dr. Stephenson is interested in theoretical aspects of transport in biological systems. Much of his recent research centers on transport of water and electrolytes in epithelia and in the kidney. One group of current studies focuses on the relation of medullary concentration gradients and the osmolality of final urine in the mammalian kidney to tubular and vascular permeabilities, flows, and architecture. A second project is to develop a mathematical model of electrolyte transport in the whole kidney, which includes electrolytes (Na^+, K^+, Cl^-, HCO_3, H_2PO_4, H^+), glucose urea, protein osmotic forces, hydrostatic pressure, and electrical potential. Approaches to these problems include both computer simulation and the development and theoretical analysis of mathematical models.

Dr. Townes-Anderson studies adult neurons of the vertebrate retina. Questions concerning synaptic mechanisms and regeneration of adult photoreceptors and secondary neurons are being addressed by examining isolated cells *in vitro*. For instance, the issue of synaptic specificity is being tested using retrogradely-labeled neurons and time-lapse video microscopy to follow the formation of synapses between

identified nerve cells types. Other projects involve the use of confocal and electron microscopy.

Dr. Weinstein is interested in the theory of solute and water transport across epithelia and developing mathematical models that permit the computer simulation of normal and pathological conditions. The primary focus of this work is the study of the proximal tubule sodium reabsorption: the transepithelial pathways and driving forces of sodium transport and the mechanisms by which physical factors modulate this reabsorption. A second focus of this research has been the dynamics of cell volume homeostasis, with scrutiny of proposed mechanisms for the coordination of solute transport at luminal and basolateral epithelial cell membranes. The most recent effort is the development of a mathematical model of the collecting duct, which will be used to simulate currently available clinical tests of distal nephron acidification.

Dr. Windhager's studies are aimed at elucidating the mechanisms of ion and water transport by renal epithelial cells, in particular the negative feedback regulation of sodium transport in cortical collecting tubules. Combining techniques of measuring transepithelial sodium fluxes, intracellular ion concentrations by fluorescence methods, and patch clamping of ion channels, it was concluded that cytosolic calcium ions and membrane voltage can account for the observed feedback control. In related studies, the renal Na/Ca exchanger has been functionally expressed in *Xenopus* oocytes and has been partially cloned. Other work is aimed at cloning the ADH-sensitive water channel in the renal papilla of the mammalian kidney.

Recent Publications

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Requirements and Course Offerings

Memorial Sloan-Kettering Cancer Center and Manhattan Skyline, as seen from Cornell Medical College.

Admission

Applications

For admission to the Graduate School of Medical Sciences an applicant must (1) have a baccalaureate degree or the equivalent from a college or university of recognized standing, (2) have adequate preparation in the chosen field of study, and (3) show promise of ability to pursue advanced study and research, as judged by his or her previous record.

As a rule, students are admitted to one of the seven programs of the Graduate School of Medical Sciences, which are: *Biochemistry, Cell Biology and Genetics, Immunology, Molecular Biology, Neuroscience, Pharmacology, and Physiology and Biophysics.* However, the initial affiliation with a program is far from rigid. For example, a student, after developing an awareness of the variety of research projects available for training, may remain in the original program but choose as thesis advisor a faculty member affiliated with another program, or the student may wish to change programs altogether.

Inquiries about graduate study should be addressed to the Associate Dean of the Graduate School of Medical Sciences, 1300 York Avenue, New York, NY 10021.

Candidates may be admitted in September, February, or July, although places in the graduate program for February and July may not be available because of prior commitments to applicants for September admission. Applicants for February or July admission should correspond directly with the respective Program Director regarding the availability of places.

Application material must be completed and returned to the Office of the Graduate School of Medical Sciences together with (1) official transcripts of records from all colleges and universities attended, (2) a statement of purpose of graduate study, and (3) two letters of recommendation from individuals in academic positions who know the applicant professionally. In addition, scores from the Graduate Record Examinations (GRE) are required to aid in the evaluation of an applicant. Application for taking the Aptitude (Verbal, Quantitative, and Analytical) Test and the Advanced Test of the GRE, must be made directly to the Educational Testing Service, Graduate Record Examinations, P.O. Box 6000, Princeton, NJ 08541-6000. Students whose native language is not English are required to take the Test of English as a Foreign Language (TOEFL). Application for this test must be made to Test of English as a Foreign Language, P.O. Box 6151, Princeton, NJ 08541-6151.

The proper Institution Code Number to use in the GRE or TOEFL application for the Cornell University Graduate School of Medical Sciences (New York City) is R 2119.

Applications for September or July admission and all credentials, including official transcripts of records from all colleges and universities attended, must be received by the **deadline of January 15.** Because GRE scores are an important part of the application it is of decided advantage to the applicant, to submit these scores by the January 15 deadline.

Applications and credentials for February admission must be received by November 1.

Application fee. A nonrefundable charge of $35 is made for filing an application for admission.

The completed application and all supporting documents are initially screened by the credentials committee of the program to which the student is applying. Applicants who are considered potentially acceptable are usually called for a personal interview. If accepted by the Program, an application is forwarded to the Dean for final decision. A student is formally notified of acceptance for study in the Graduate School of Medical Sciences by a letter from the Dean. An applicant accepted for admission is requested to promptly inform the Graduate School of Medical Sciences of her or his plan to either accept or refuse the offer of admission.

It is the policy of Cornell University to actively support equality of educational and employment opportunity. No person shall be denied admission to any educational program or activity or be denied employment on the basis of any legally prohibited discrimination involving, but not limited to, such factors as race, color, creed, religion, national or ethnic origin, sex, age, or handicap. The University is committed to the maintenance of affirmative action programs which will assure the continuation of such equality of opportunity.

Admission policies are also in conformity with the policy of New York State in regard to the American ideal of equality of opportunity as embodied in the Education Practices Act.

Categories

An applicant is accepted by the Graduate School of Medical Sciences (1) as a degree

candidate for the MS or PhD, or (2) as a provisional candidate.

Provisional candidacy permits a prospective degree candidate, whose educational preparation is difficult to evaluate, to begin graduate studies. On the basis of the record of accomplishment in the first half of the academic year, the adviser or temporary Special Committee of a provisional candidate may recommend to the Dean that (1) provisional candidacy be changed to degree candidacy, (2) provisional candidacy be continued for the remainder of the academic year, or (3) provisional candidacy be terminated. A maximum of one academic year in the status of provisional candidacy is permitted and credit of a maximum of one residence unit may be allowed on petition, provided there is convincing evidence that performance has been of the same quality as that required of degree candidates.

Special Students

Special students are students who are not degree candidates in the Graduate School of Medical Sciences and who are given permission by the Dean to take courses at Graduate School of Medical Sciences. Special students must be degree candidates at other institutions and the courses taken at Cornell must be essential to their degree programs and are not offered by the institutions in which they are matriculated as degree candidates, as certified by the institutions. Enrollment as a special student is not intended as preparation for admission to degree programs at Cornell or elsewhere.

Special students are accepted only with the approval of the appropriate Program Chairperson. Such students must demonstrate special qualifications in terms of preparation and ability. They must register with the Graduate School of Medical Sciences and must pay all tuition and fees before being permitted to attend lectures or laboratory sessions. Tuition is computed on the basis of the ratio of course hours taken to the total hours of instruction for the academic year (33 weeks of 40 hours). There is a registration fee of $35.

Degree Requirements

Major and Minor Programs

A candidate for the degree of Master of Science is required to register for study in one major and one minor program. Each program decides whether the Special Committee of a candidate for the PhD degree must have two or three programs represented. Accordingly, a candidate for the degree of Doctor of Philosophy is required to register for study in one major and one or two minor programs. At least one of the minors must be outside the area of the major program.

The Special Committee

The general degree requirements of the Graduate School of Medical Sciences are minimal in order to give maximum flexibility in choosing a desirable program of study. The student's program is determined with the aid and direction of a Special Committee, consisting of at least three faculty members chosen by the student from those programs that best fit his or her areas of interest. Satisfactory progress toward a degree is judged by the committee rather than by arbitrary standards imposed by the Graduate School of Medical Sciences. There are no regulations of the Faculty of the Graduate School of Medical Sciences governing the specific content of instruction, courses, or grades to which the Special Committee must subscribe, except those imposed by the programs. The committee is primarily responsible for the candidate's development as an independent scholar and scientist.

No later than four weeks after enrollment, a candidate must file a statement of the major and minor programs elected for study, after which the student must choose faculty members to represent the programs and to serve on a Special Committee. The major sponsor usually advises the student concerning the other selections and chairs the committee. At least one member of the committee must represent a program different from the candidate's major program. Members may agree to serve temporarily during the candidate's first year of residence until the candidate has had the opportunity to become acquainted with areas of research in the programs of his or her choice. On completion of this year of residence, a permanent Special Committee will be formed, the membership of which can be changed with agreement of all members of the old and newly formed committees and the approval of the Dean. The members of the Special Committee decide on the student's program of study and research. They judge whether progress toward a degree is satisfactory and prepare term reports on the candidate for submission

to the Dean. The members of the committee serve on all the candidate's examining committees and they approve his or her thesis.

Registration and Course Grades

No student in the Graduate School of Medical Sciences may double-register for an advanced general or professional degree with any other school or college except the Cornell University Medical College.

At the beginning of each term, students are required to register with the Office of the Graduate School of Medical Sciences and to file a registration of courses form indicating all courses they will take. A fee of $10 is charged for late registration.

At the beginning of each course in which the student is enrolling, the student will complete a separate course registration form for the instructor. All courses for which the student registers for credit will be entered in the official record. Grades of graduate students are reported as: Excellent (E), Satisfactory (S), Unsatisfactory (U), Incomplete (I), Absent (Abs.), or Unofficially Withdrawn (W). A grade of Incomplete or Absent cannot be changed later than one term following the term in which the course was taken.

Registration for the summer is required of graduate students who will be engaged in research.

Residence

The Faculty of the Graduate School of Medical Sciences regards study in residence as essential. Each candidate for an advanced general degree is expected to complete the residence requirements with reasonable continuity. A student must register each term from the time of his or her first registration in the Graduate School of Medical Sciences until the student either withdraws or completes a degree (unless a leave of absence has been granted). Full-time study for one-half academic year with satisfactory accomplishment constitutes one residence unit. Two units of residence are the minimal requirement for the masters degree and six units are the minimum for the doctoral degree. However, the time necessary to obtain the degree generally exceeds the minimal requirements. A candidate for the PhD degree must spend two of the last four units of required residence in successive terms on the New York City or the Ithaca campus of Cornell University. No more than seven years may intervene between the time of first registration and the completion of all requirements for the doctoral degree. A student must complete all requirements for the master's degree in four years.

Part-time graduate study, if it is necessitated by off-campus employment noncontributory to the major program of study, is not encouraged. Requests for part-time study must be reviewed by the Executive Committee. If permission is granted for part-time study, the student must be in residence at least half-time.

Transfer of Residence Credit

No residence credit will be granted for study outside the Graduate School of Medical Sciences to fulfill the requirements of the MS degree. No commitment can be made about granting residence credit toward the PhD requirements for previous study in another graduate school until after the candidate has entered into residence at the Graduate School of Medical Sciences. At that time, the student's Special Committee may recommend acceptance of study outside the Graduate School of Medical Sciences to the Executive Committee, which will determine the number of residence units to be awarded. No credit can be transferred for study undertaken as an undergraduate or as a special student even in courses designed for graduate students.

A student who has satisfactorily completed two or more academic years of study toward the MD degree at the Cornell University Medical College, or another accredited medical school in the United States with a curriculum equivalent to that of the Cornell University Medical College, may transfer a maximum of two units of residence credit after passing an evaluation examination administered by a committee appointed by the Executive Committee of the Graduate School of Medical Sciences.

Summer Research

Registration is required for the summer research term whether or not this effort will be credited toward residence unit accumulation. Students registered for summer research pay prorated tuition only if they are obtaining residence credit. However, no degree candidate is eligible for more than two residence units in any period of twelve consecutive months.

Study *In Absentia*

A candidate for the degree of Doctor of Philosophy may petition for permission to earn residence units for study away from Cornell University while regularly registered in the Graduate School of Medical Sciences. A candidate to whom this privilege has been granted, must register as a Candidate *in absentia* and may work temporarily under the immediate supervision of an individual designated by his or her Special Committee although the candidate's program will continue to be directed by the Committee. For study *in absentia* not more than two residence units may be earned toward fulfillment of the minimal residence requirements for the PhD degree.

Leave of Absence

A candidate who finds it necessary to interrupt the continuity of his or her residence must petition the Dean for an official leave of absence. This written petition must specify the term of absence, state the reason for the requested leave of absence, and be approved by the student's major sponsor.

Candidacy for Degree Only

A graduate student who has fufilled all degree requirements, with the possible exception of the thesis defense and final thesis submission, who leaves campus and is no longer a full-time student, is granted Candidate for Degree Only status, which is in effect until graduation.

Examinations

Three examinations are required by the Faculty of the Graduate School of Medical Sciences: (1) Final Examination for the MS degree, (2) Examination for Admission to Doctoral Candidacy, and (3) Final Examination for the PhD degree. Examinations are administered by an Examining Committee consisting of a chairperson appointed by the Dean, the members of the candidate's Special Committee, and, in the case of the Admission to Doctoral Candidacy Examination, one additional member selected from the Faculty of the Graduate School of Medical Sciences or of other institutions. In addition to these examinations, the candidate's major program may require a qualifying examination as part of its evaluation of the candidate after two units of residence have been completed.

For the MS degree: The Final Examination may be oral or both oral and written.

For the PhD degree: The Admission to Doctoral Candidacy Examination is both oral and written and certifies that the student is eligible to present a thesis to the Faculty of the Graduate School of Medical Sciences. The examination should be taken after course work is largely finished but before significant thesis research has begun. Accordingly, the usual examination time will be at the end of the second year of residence. The examination may not be taken until two units of residence credit have been accumulated and a minimum of two units of residence credit is required after passing this examination before the final examination can be scheduled. The final examination for the PhD degree is an oral defense of the candidate's thesis. It must be passed within four years after completion of the required residence units, or within seven years from the date of first registration, whichever is earlier.

Thesis

A principal requirement for both the MS and the PhD degrees is the presentation of a thesis constituting an original contribution to knowledge. Ordinarily, the thesis is written on a research topic in the candidate's major field of study, under the direction of the chairperson of his or her Special Committee. The time between the thesis defense and submission of the thesis in its final form is limited to 60 days. The faculty requires that the PhD thesis be published in abstract and be recorded on microfilm.

Tuition and Fees

Tuition

Tuition for a student regularly matriculated in the Graduate School of Medical Sciences is $15,380 for the academic year 1993–94 and is payable in two equal parts, the first of which is due at initial registration. Tuition includes fees for matriculation, the student health plan, graduation, and miscellaneous thesis expenses.

Students in the PhD-MD program (see pp. 4 and 72) will be charged Medical College tuition while they are enrolled in medical school.

A student who is to receive partial residence credit (see p.66) because of

employment should apply for proration of tuition on forms obtainable at the Office of the Dean.

Other Fees

In Absentia A student registered *in absentia* pays a fee of $200 each term.

Leave of Absence Students on leave of absence will be required to pay an active-file fee of $200 for each semester, up to a maximum of six semesters, during which they are not registered with the Graduate School. This fee will not be subject to finance charges but must be paid before the student can receive an advanced degree. Petition for waiver of this fee will be considered for students who have not completed the required number of residence units.

For students on leave of absence, the student health plan will remain in force for 30 days following the commencement of the leave.

Candidacy for Degree Only A student who registers as a Candidate for Degree Only pays a one-time fee of $35.

Any individual who owes money to the University will not be allowed to register or reregister in the University, receive a transcript of his or her record, have his or her academic credits certified, be granted a leave of absence, have a degree conferred, and will not be eligible for health services and subsidized housing.

The amount, time, and manner of payment of tuition, fees, or other charges may be changed at any time without notice.

Refunds

Part of the *personally* paid tuition will be refunded if the student obtains official certification of leave of absence or withdrawal from the Graduate School of Medical Sciences during the semester. Students who terminate their registration during a regular term in this manner will be charged tuition from the registration day to the effective date of the certificate as follows: first week, 10 percent; second week, 20 percent; third week, 30 percent; fourth week, 40 percent; fifth week, 60 percent; sixth week, 80 percent; seventh week, 100 percent. No charge will be made if the effective date of leave or withdrawal is within the first six days of the term, including registration day.

Financial Assistance

Students who wish to apply for a Stafford Student Loan or other Federal assistance are required to submit a Free Application for Federal Student Aid (FAFSA) for an estimate of financial need. Application forms can be obtained from the Graduate School Office.

Financial assistance is available to qualified applicants. Individual programs may offer predoctoral research fellowships, research assistantships, or teaching assistantships. These positions may provide a stipend in addition to tuition. Information about these positions may be obtained directly from the Program Director at the time of application.

Nationwide competitive predoctoral fellowships are available from the National Science Foundation, the National Research Council, and the Howard Hughes Medical Institute. Information about these fellowships should be requested directly from the appropriate agency.

New York State residents are eligible for several predoctoral fellowships and the Tuition Assistance Program. Application forms may be obtained from the New York Higher Education Services Corporation, Student Financial Aid Section, Tower Building, Empire State Plaza, Albany, NY 12255.

Several other loan programs are available to graduate students. Under these programs, repayment of the principal amount of the loan together with the interest on the loan may be deferred until after graduation. Complete information regarding loan programs may be obtained from the Graduate School Office.

Opportunity for part-time employment is often available in departmental research projects or other activities. Applications should be made directly to individual departments.

Scholarships and Fellowships

Full fellowships are available for graduate students. Recipients of this award become PhD Fellows and will receive a full tuition scholarship and a stipend covering living expenses.

Tuition scholarships are available for students who are not covered by a fellowship. This scholarship fund is administered

by the Office of the Dean of the Graduate School of Medical Sciences.

In addition, the following named funds provide support for selected students:

The Vincent Astor Scholarship Fund. Funds for tuition assistance are also derived from the income from a generous gift by the Vincent Astor Foundation to the Graduate School of Medical Sciences and to the Medical College. Allocation of these funds for graduate student tuition assistance is made at the discretion of the Dean of the Graduate School of Medical Sciences.

The Departmental Associates Fellowship was established by the generous contributions of The New York Hospital-Cornell Medical Center Departmental Associates for the support of a PhD candidate in the Cornell University Graduate School of Medical Sciences.

Herbert and Lee Friedman Fellowship provides support for an MD-PhD student and is funded through income derived from an endowment established by Mr. Herbert Friedman to the Sloan-Kettering Institute.

Lee Friedman Memorial Fellowship. Funds for the support of an MD-PhD student are provided by income generated from an endowment to the Sloan-Kettering Institute in memory of Lee Friedman, the wife of Herbert Friedman.

The Harry E. Gould, Sr., Medical and Graduate Student Scholarship. This fund was established by Mr. Gould's son, Harry E. Gould, Jr., in memory of his father, a prominent business and civic leader in the City of New York who had a long-standing interest in medicine. The income from this endowment provides financial assistance for students of the Medical College and Graduate School of Medical Sciences.

The Mildred and Emil Holland Scholarship. Income from a gift by the Emil and Mildred Holland Philanthropic Fund of the Jewish Communal Fund is used to provide tuition support for an MD-PhD student.

The Frank L. Horsfall, Jr., Fellowships are derived from income generated by the Frank L. Horsfall, Jr. Fund and are awarded each year to two outstanding students sponsored by faculty members of the Sloan-Kettering Institute.

Robert W. Johnson, Jr., Charitable Trust. The income on a permanent endowment to the Sloan-Kettering Institute provides a fellowship for an MD-PhD student.

The W. M. Keck Foundation Medical Scientist Fellowship. This award is derived from a generous endowment awarded to Cornell University Medical College and provides support for an MD-PhD student.

The Frances L. Loeb Medical Scientist Fellowships. These fellowships have been endowed by a gift from Frances L. Loeb and provide support for two MD-PhD students at the Cornell University Medical College.

The Shirley L. Marshak Fellowship is funded by income derived from the Shirley L. Marshak Trust for Charities. The fellowship has been designated for award to a student of the Graduate School of Medical Sciences who is engaged in biomedical research.

The Andrew W. Mellon Foundation Fellowships. A grant by the Andrew W. Mellon Foundation provides fellowship support for MD-PhD students selected for the Tri-Institutional Medical Scientist Training Program which is administered jointly by Cornell University Medical College, the Cornell University Graduate School of Medical Sciences, and The Rockefeller University.

The Frank R. and Blanche A. Mowrer Memorial Fund. Financial assistance is available from the income of this fund to one student each year enrolled in the PhD-MD or MD-PhD program.

The Papanicolaou Medical Scientist Fellowship is funded by income from a bequest from Mary G. Papanicolaou in memory of her husband, Dr. George N. Papanicolaou, and by a gift from an anonymous donor to the Cornell University Medical College. The funds provide support for an MD-PhD student.

The Abby Rockefeller Mauzé Medical Scientist Fellowship was established by a gift from the Abby Rockefeller Mauzé Trust. The income provides fellowship support for an MD-PhD student.

Louis and Rachel Rudin Foundation. The generous gift to the Sloan-Kettering Institute from the Foundation provides a fellowship for an MD-PhD student.

The Surdna Foundation Medical Scientist Fellowship was made possible by a generous grant to the Medical College by the Surdna Foundation. The income from this endowment provides fellowship support for an MD-PhD student.

The Iris L. and Leverett S. Woodworth Medical Scientist Fellowship. Funds for the support of an MD-PhD student are provided by the income from a generous gift from Dr. Leverett S. Woodworth in his own name and in memory of his wife, Iris L. Woodworth.

Gateways to Science Program. With generous funding by the Departmental Associates of the New York Hospital-Cornell Medical Center, the Cornell University Graduate School of Medical Sciences has implemented a program which will provide minority college students with summer research opportunities in laboratories of Cornell University Medical College and the Sloan-Kettering Institute. The aim of the program is to foster an interest in biomedical research in minority students at all college levels. The grant enables the school to provide a two-month stipend and subsidized housing for qualified students.

Awards and Prizes

The Julian R. Rachele Prize. The income of a fund established by Dr. Julian R. Rachele, former Dean of the Cornell University Graduate School of Medical Sciences, provides for an annual prize to be awarded to a candidate for the PhD degree for a research paper of which the candidate is the sole or the senior author.

The prize was awarded in 1993 to Marcus Bosenberg.

The Vincent duVigneaud Prizes for the presentation of outstanding papers by students of the Cornell University Graduate School of Medical Sciences at the Annual Vincent duVigneaud Memorial Research Symposium.

Recipients of these awards in 1993 were Iris Alroy, Rajat Bannerji, Marcus Bosenberg, Marina Brodsky, Annick Le Gall, John Prescott, and Killu Tougu.

Student Health Services

The student Health Plan of Cornell University Medical College provides hospitalization and major medical insurance for all registered graduate students. In addition, the Plan provides for ambulatory care at the Student Health Service of The New York Hospital Cornell Medical Center. Physicians at the Health Service will refer students who require specialized care to clinics of the New York Hospital and to attending physicians when needed.

The cost of medical services provided by the Plan is included in the tuition and fee structure announced by the Graduate School of Medical Sciences each academic year. Students will be issued Plan membership cards and will receive courtesy privileges at The New York Hospital Pharmacy.

Entering students are requested to have a physical examination, tuberculosis skin test and laboratory tests performed by their personal physicians prior to matriculation. The hours of the Student Health Service and a complete statement of Plan benefits will be provided to each graduate student upon arrival.

It is recommended that students purchase insurance coverage for eligible dependents who do not have other insurance available to them. Insured dependents are not eligible for care at the Student Health Service but they will be referred to appropriate members of the Hospital staff for medical treatment.

Students who withdraw from the Graduate School of Medical Sciences will be covered for 30 days from the effective date of withdrawal. Dependent coverage may also be continued for this period, and costs will be prorated from the date of termination. See the Registrar of the Medical College to make such arrangements.

Students on an academic leave of absence from the Graduate School of Medical Sciences will be covered for 30 days after the official commencement date of the leave. Dependent coverage may be continued for this period, and costs will be prorated from the date of termination. Students on medical leave of absence from the Graduate School of Medical Sciences will be fully covered for the duration of the academic year.

Graduating students and their dependents are covered until the last day of the month following the month in which the student was last registered in the Graduate School of Medical Sciences.

Residence Halls

F. W. Olin Hall, a student residence, is at 445 East Sixty-ninth Street, directly across from the Medical College entrance on York Avenue. Olin Hall contains a gymnasium, lounges, a kitchen on each student floor, and 200 residence rooms. Each room is a single bedroom-study, completely furnished. Two adjacent rooms share a connecting bath. The housing fee for the 1993–1994 academic year is $292 per month.

Livingston-Farrand Apartments, also located on East Sixty-ninth Street, just beyond Olin Hall, have furnished studio, one-bedroom, and two-bedroom apartments. Kitchen facilities are provided in these apartments. Housing fees begin at $382 per month (utilities not included). These apartments are available to families and upper-class students.

Jacob S. Lasdon House, an apartment residence, is located at 420 East Seventieth Street. This building contains studio, one- bedroom, and two-bedroom apartments, and two squash courts. Apartments are fully furnished, include kitchens, and are centrally air conditioned. Housing fees for students sharing apartments begin at $339 per month including utilities. Fees for families begin at $635 including utilities. These apartments are available to families and upper-class students.

303 E. 71st Street Apartments. A limited number of furnished apartments, operated by the Memorial Sloan-Kettering Cancer Center, is available for students of the Cornell University Graduate School of Medical Sciences. Rental rates are $716 and $913 for one- and two-bedroom apartments, respectively.

Housing in the above facilities is guaranteed for a five-year period from the time of first enrollment.

The fees listed may be changed at any time without previous notice.

Pets are not permitted in student housing.

Special Programs

Application to the Tri-Institutional MD-PhD Program

See pp. 3 and 84 for a description of the program. A successful applicant will demonstrate excellent undergraduate science preparation and a strong commitment to combining an investigative career in the biomedical sciences with clinical medicine. Applicants must satisfy the requirements of each institution. After initial screening, selected candidates will be invited to meet with members of the faculties of the medical and graduate programs.

To complete an application, students must submit the following:

To AMCAS in Washington, D.C.:

1. *AMCAS Application.* A completed AMCAS application form should be sent directly to AMCAS by October 15. The personal data and academic record required are suitable for evaluation by both the medical and graduate schools.

To the Tri-Institutional MD-PhD Program, Cornell University Medical College, 1300 York Ave., New York, NY 10021:

2. *MD-PhD Application Form.* The Tri-Institutional Program Application Form will be sent when information about the program is requested.
3. *Test Scores.* MCAT scores are required; GRE scores are optional.
4. *Personal statement.* Candidates should submit a personal statement summarizing their research background and scientific interests, as well as reasons for wishing to pursue the combined degree.
5. *Letters of Recommendation.*
   a. Each applicant should arrange to provide either a statement and supporting material from his or her premedical advisory committee, or two letters from undergraduate science faculty members evaluating the candidate's suitability for a career in medicine.
   b. Letters from at least two faculty members evaluating the candidate's research potential should also be submitted.
6. *Application Fee.* A $50 processing fee will be requested when the AMCAS application is received by the Medical College Office of Admissions. This fee can be

waived in cases of financial hardship. There is no additional application fee for the MD-PhD Program.

Deadline. Applications must be received by **November 30.**

Application to the PhD-MD Program

See p. 4 for a description of the program. Students admitted to the program will matriculate as second-year medical students, following successful completion while enrolled in the Graduate School of Medical Sciences (GSMS) of all first-year courses of Cornell University Medical College (CUMC) and of all requirements for the PhD degree.

Application for admission to CUMC can be made either during the academic year preceding the year of anticipated enrollment, or two years prior to enrollment. Students must have passed the Admission-to-Doctoral-Candidacy Examination and at least two major first-year medical school courses by the time application is made. Admission, if granted, will be conditional pending completion of all requirements for the PhD degree and of all remaining first-year medical school courses.

To complete an application, students must submit, **by October 15,** the following documents to the Office of the Dean of the GSMS:

1. A completed application for admission with advanced standing (second year) to CUMC. Application forms are obtainable from the CUMC Admissions Office.
2. An up-to-date transcript from the GSMS showing successful completion of at least two *major* courses of the first-year medical school curriculum (Biochemistry, Gross Anatomy, Cell Biology and Microscopic Anatomy, Physiology and Biophysics, Neuroscience).
3. A plan of study for the remaining years in graduate school, incorporating all courses of the first-year medical school curriculum still to be taken. The plan must show endorsing signatures of the members of the student's Special Committee.
4. Two letters of recommendation, one by the student's major sponsor, and one by another member of the faculty of the GSMS addressing the applicant's suitability for PhD-MD program.
5. Results of the Medical College Admissions Test (MCAT).

The Office of the Dean of the GSMS will review the student's credentials and make a recommendation to the Committee on Admissions of CUMC. After review of the application and personal interviews, this committee will determine the acceptability of the student for the MD-PhD program and will inform the student of its decision before June 1.

After completion of the second and third years and the required selectives of the fourth year of the Medical College, students in the program receive credit for their graduate studies to satisfy the elective requirements of the fourth-year Medical College curriculum.

While registered as graduate students, the PhD-MD candidate is subject to the tuition schedule of the GSMS. Upon registration at CUMC, the candidate is responsible for the tuition charged by the Medical College (full tuition for the second and third years, and a minimum of 30% of the fourth-year tuition).

Biochemistry

Graduate Program Chairman

Esther M. Breslow, Department of Biochemistry, Cornell University Medical College, Room E-219, 1300 York Avenue, New York, NY 10021, (212) 746-6405

Graduate Program Director

David P. Hajjar, Department of Biochemistry, Cornell University Medical College, Room A-626, 1300 York Avenue, New York, NY 10021, (212) 746-6470

Graduate instruction is offered leading to the PhD degree. Within the framework of degree requirements and in consultation with the student, the course of study is planned to fit the need of the individual. Although formal course work is required, emphasis is placed on research. Research opportunities exist in various areas of biochemistry including enzymology, structure and function of proteins and nucleic acids, molecular biology, physical biochemistry, and the intermediary metabolism of amino acids, carbohydrates, nucleic acids, and lipids. Entering graduate students rotate for periods of two or three months in the laboratories of different faculty members of the Program before beginning their thesis research. Students are encouraged to choose challenging fundamental research problems that are on the frontiers of biochemistry.

The laboratories of the faculty members are equipped with the instrumentation required for modern biochemical research. Graduate students are instructed in such methodology as high performance liquid chromatography, protein sequencing and amino acid analysis, recombinant DNA technology (including nucleic acid sequencing and the polymerase chain reaction), radioactive isotope techniques, electrophoresis, and circular dichroism and other spectroscopic methods.

Students who undertake graduate study in biochemistry must have a sufficiently comprehensive background in chemistry to pursue the proposed course of study and must present evidence of knowledge of biology, general experimental physics, and mathematics. Students may remedy deficiencies in these areas during the summer before entering graduate school, or in some cases, during the first year of graduate study. The Graduate Record Examination (the aptitude test and the advanced test in chemistry or biochemistry) is ordinarily required.

Course requirements: In the first year, students take the Biochemistry course for graduate and medical students, given in the first two quarters, and the graduate Biochemistry course, given in the third quarter. In addition, all students are required to participate in Journal Club. No other courses are required, but graduate students generally encouraged to select additional courses in Biochemistry, in their minor program, or in other programs, in consultation with the members of their Special Committee. Students in the MD-PhD program are required to complete the first two years of the medical school curriculum and the Frontiers in Biomedical Science course. The Graduate Biochemistry course and/or other graduate courses may be recommended by the student's Special Committee, depending on the student's background and interests.

Courses

Biochemistry. This course is designed to provide the student with a knowledge of the fundamentals of biochemistry and an appreciation of the molecular basis of biological phenomena. There is an emphasis on the biochemical and molecular events relevant to human health and disease. The course is offered to both graduate and medical students. Topics covered include chemical and physical properties of biomolecules, enzymology, molecular biology, metabolism of carbohydrates, lipids, amino acids, purines, and pyrimidines. Graduate students in the Program in Biochemistry are required to pass this course (or its equivalent). First and second quarters, annually. Dr. Tate, Dr. Wellner, and staff.

Graduate Biochemistry. This is a research-oriented course which examines in detail the structure of proteins and the experimental methods available for increasing our understanding of these important macromolecules. Topics include modern methods of protein isolation and structure

determination. Also covered will be techniques for studying protein conformation and interaction with ligands such as substrates, coenzymes, and hormones. Graduate students in the Program in Biochemistry are required to pass this course (or its equivalent). Third quarter, annually. Dr. Wellner and staff.

Membrane Biochemistry. This course consists of a series of 15 lectures covering topics on structure-function relationships during membrane biogenesis and cell-cell interactions. Topics include membrane composition, membrane cell biology, physical techniques to study membrane structure, membrane receptors and stimulus-response coupling, membrane pathophysiology, thermodynamics, and the molecular aspects of membrane fluidity. These topics will be taught assuming that students have taken the first year Biochemistry course (or its equivalent). Fourth quarter, 1994–95. Dr. D. Hajjar.

Journal Club. This meets twice a month during the academic year and is required for all graduate students. Students and postdoctoral fellows meet, with faculty supervision, to discuss recent papers of biochemical importance. Student participation involves the presentation of papers and critical discussion of their contents and significance. Dr. Anderson and Dr. Cooper.

Other Academic Offerings

Introduction to Research. Laboratory rotations in experimental biochemistry dealing with the isolation, synthesis, and analysis of substances of biochemical importance (enzymes, proteins, nucleic acids, lipids, and metabolic intermediates), and study of their properties by various chemical and physical techniques. The student obtains this varied research experience by spending approximately two months in the laboratory of each of four faculty members of his or her choice. For incoming graduate students majoring in biochemistry.

Biochemistry Seminars. A seminar series in which students, faculty, and invited scientists from this and other institutions report on progress in their laboratories.

Cell Biology and Genetics

Graduate Program Co-Chairmen

Joan Massagué, Sloan-Kettering Institute, Cell Biology & Genetics Program, 1275 York Avenue, New York, N.Y. 10021, (212) 639-8975

Enrique Rodriguez-Boulan, Department of Cell Biology & Anatomy, Cornell University Medical College, 1300 York Avenue, New York, NY 10021, (212) 746-6158

Graduate Program Director

David M. Bader, Department of Cell Biology & Anatomy, Cornell University Medical College, 1300 York Avenue, New York, NY 10021, (212) 746-6149

The Program in Cell Biology and Genetics offers advanced study leading to the PhD degree. The program is intended to prepare students for a career in basic research and teaching in cell or developmental biology, genetics, molecular biology, or related disciplines.

Course Requirements: In the first two years students are expected to complete a core curriculum of Graduate Biochemistry, Cell Biology, and Molecular Genetics. First year students also participate in a formal journal club designed to foster skills in literature comprehension and oral presentation. To satisfy the requirements for the PhD, the students also select four quarters (one year) of elective courses chosen to complement their background and develop their interests.

At the end of the first year, an oral evaluation of each student is conducted in order to monitor student progress and identify areas of strength and weakness. Students are also urged to participate in a weekly forum in which they and postdoctoral fellows report on their research, and are expected to attend one of the weekly research symposia hosted by the departments of Cell Biology & Anatomy or Cell Biology & Genetics. Although the official transcript reports only three grade levels, students are expected to perform at a level corresponding to a B average.

Laboratory Rotations: Students rotate through three laboratories during the first year. Such rotations familiarize students with ongoing research in the Program and provide a mechanism for selection of the thesis sponsor. Written rotation reports also

provide practice in the skills of presenting scientific data.

Admission to Doctoral Candidacy: The Program administers a qualifying examination before the end of the second year of residence. The specific format of the examination, which is composed of written and oral sections, is determined by the examining committee. Typically, the written examination covers three or four topics selected by the student and committee, and the oral examination centers around a brief research proposal on a topic chosen by the student and not related to the thesis project.

Courses

Advanced Cell Biology. This course is organized as a combination of biweekly lectures, small group discussions in which students present and discuss key papers in cell biology, and research seminars by experts in appropriate fields. The course covers topics of current interest in cell biology in the areas of cytoskeleton and cell motility, cell cycle, cytoplasmic organization, cell-cell and cell-extracellular matrix interactions, protein sorting, organelle biogenesis, receptor structure and function and second messenger systems. Offered third and fourth quarters annually. Dr. Pardee and staff.

Molecular Genetics. The class focuses on key topics of molecular genetics in bacteria and bacterial viruses, yeast, nematodes, *Drosophila*, mouse, mammalian cells in culture and their viruses. Topics may include chromosome structure, transcriptional and translational regulation, genomic plasticity and elements of genetic diversity. The isolation of mutants and their analysis by recombination, complementation and the generation of suppressors are discussed in depth. The course consists of lectures and interactive small-group discussions of research papers from the current literature. Limited to 36 students. Offered as two sequential two-quarter courses, with the first half focusing on basic concepts, prokaryotic and simple eukaryotic systems, and the second half covering complex eukaryotic systems and special topics. Quarters I and II: Drs. Ballinger, Caudy, Holloman, Lustig, Osley and Traktman. Quarters III and IV: Drs. Ballinger, Dorsett, Jasin, and Lacy.

Developmental Biology. Principles of descriptive, experimental, and molecular developmental biology are presented, using several animal systems as examples. Early development of the whole organism and of cells, tissues, and organs are considered. Prerequisites: consent of the faculty. Limited to 15 students. Offered in alternate years; third and fourth quarters in 1994–95. Drs. Bachvarova and Bader.

Practicum in Biological Optics. A workshop in practical aspects of light and electron microscopy. Following a weekly lecture, students conduct specific protocols involved in light and electron microscopy. Topics covered include: tissue fixation, embedding and thin sectioning; transmission and scanning electron microscopy; shadow-casting of proteins and nucleic acids; immunocytochemistry; fluorescence, phase and interference microscopy; laser-scanning confocal microscopy; image reconstruction; photography. All participants are required to complete an independent project. Prerequisite: consent of instructors. Course requirements include the completion of an independent project paper. Limited to 10 students. Offered in alternate years; third and fourth quarters in 1994–95. Ms. Cohen-Gould, Dr. Fischman, and staff.

Biophysics for Biologists. In this new course, concepts and methodological approaches in biophysics will be applied to current research problems in cell biology and physiology, emphasizing molecular structure and function. The course will be offered annually with alternating subject material. In 1994, the course will address the structure, dynamics and function of membrane lipids and proteins. Two combined lecture and research paper discussions per week. Fourth quarter, Drs. Andersen, Breslow, Pardee, Roepe, and Scotto.

Medical Genetics. This course covers aspects of human genetics in depth. The course will present lectures by the faculty and guest speakers on topics which explore the organization of the human genome, gene mapping and linkage, cytogenetics, genetic factors that contribute to normal human variation, inherited and *de novo* genetic alterations that lead to disease states, and application of genetic knowledge to clinical medicine. Dr. Chaganti and staff. Offered in alternate years; first and second quarters in 1993–94.

Journal Club Seminar for First-Year Students. This seminar is designed to give first-year students a chance to improve their skills in presenting and analyzing scientific data. Each student presents two papers during the semester. Papers are chosen by the students and approved by the instructors. Speakers generally provide a brief relevant background and then present each figure in the paper, summarizing the experimental method or assay used, the results illustrated, and the conclusions drawn. Participation by all students is encouraged during the presentation. Given jointly with the Molecular Biology program. Offered annually, third and fourth quarters. Drs. Caudy, O'Donnell, and Shuman.

Graduate Student Seminar. This informal seminar is designed to improve graduate students' skills in public presentation. On a rotating basis, students prepare an oral presentation on their research or on a topic of their choice.The presentation is informally critiqued by the faculty. First through fourth quarters, annually.

Cell Biology and Microscopic Anatomy. Offered by the staff of the Program in Cell Biology and Genetics in conjunction with the Faculty of the Cornell University Medical College.This course follows a cellular and differentiative approach aimed at understanding the structure-function correlates that characterize the different tissues and organs. Lectures are complemented by small-group discussions and laboratory exercises designed to provide students with the skills to study and analyze cells and tissues. A microscope slide collection, presenting tissues and organs in a variety of physiological and developmental states, as well as correlative electron micrographs, are provided for individual study in the laboratory. Second and third quarters, annually. Drs. Brown and Falcone.

Gross Anatomy. Regional anatomy is studied principally through dissection of the human body. Supplementing this technique are prosections by instructors, tutorial group discussions, and radiographic and endoscopic demonstrations. Enrollment is limited and students should consult the staff early in order to determine the availability of places. First and second quarters, annually, Drs. Hagamen and Weber, and the staff.

Immunology

Graduate Program Co-Chairmen

Kenneth O. Lloyd, Sloan-Kettering Institute, Immunology Program, Kettering Laboratory, 1275 York Avenue, New York, NY 10021, (212) 639-2257

Kendall A. Smith, Department of Medicine, Cornell University Medical College, 1300 York Avenue, New York, NY 10021, (212) 746-4464.

Graduate Program Director

Janet S. Lee, Sloan-Kettering Institute, Immunology Program, 1275 York Avenue, New York, NY 10021, (212) 639-8252

The program of study is developed for each student individually on the basis of the student's interest and prior experience. Immunology students generally take a core of formal courses offered by the graduate school in immunology, biochemistry, molecular biology, cell biology and genetics in order to complement their previous background and fulfill their own academic objectives. Participation in a graduate student seminar course is expected of all students to provide experience in oral presentation.Admission to Doctoral Candidacy at the end of the second year requires both written and oral examinations of the candidate's general understanding of immunology and related subjects which are relevant to the proposed research. However, the main focus of the graduate program in immunology is on laboratory research. Each student is required to undertake at least two minor research projects with different faculty members prior to developing a major research proposal for the doctoral thesis.This allows for laboratory experience to begin during the first year of the student's program. By the third year the doctoral candidate begins a full-time thesis project which typically takes two to three years. During this time the student will continue to participate in the other educational programs offered by the Institute.These include a wide variety of research seminars which are offered throughout the year with speakers from outside the Institute. In addition, the Immunology Program offers a series of colloquia on current topics in immunology with presentations and discussions led by Immunology faculty members.

Applicants should have a strong undergraduate background in the biological sciences, including biochemistry, molecular genetics and microbiology and are also expected to have

some undergraduate laboratory research experience.The application requires a personal statement describing the student's background and specific interest in the Immunology Program. An official transcript of the student's undergraduate record is also necessary with at least two letters from faculty members who can evaluate the academic potential of the student in a PhD program in Immunology. Applicants must also submit the results of the Graduate Record Exam including the advanced test in Biology or Chemistry.

Courses

Immunology. This course provides a comprehensive overview of basic immunology with a focus on recent developments in many areas. There is an emphasis on current papers and experimental approaches to the study of immunology.

Topics include techniques in immunology, B lymphocytes, immunoglobulins and monoclonal antibodies,T lymphocytes and T-cell clones, immunogenetics of lymphocyte differentiation antigens, cell mediated immunity,T cell antigen receptors, natural cytotoxicity, macrophage and other accessory cells, lymphokines, and the major histocompatibility complex genes. Quarters I–IV, annually. Dr. Lee and the Immunology Program Faculty.

Other Academic Offerings

Colloquia in Immunology. Informal sessions are held monthly between students and senior faculty members to acquaint students with the major research programs headed by each of the faculty members of the Immunology Program.

Student Seminar Series. Graduate students have an opportunity to present their work in an informal setting. Quarters I—IV, annually.

Molecular Biology

Graduate Program Co-Chairmen

Kenneth I. Berns, Department of Microbiology, Cornell University Medical College, Room B-308, 1300 York Avenue, New York, NY. 10021, (212) 746-6505

Kenneth J. Marians, Molecular Biology Program Sloan-Kettering Institute, Room 1101A, Rockefeller Research Laboratory, 430 E. 67th Street, New York, NY 10021, (212) 639-5890.

Graduate Program Director

Mary Ann Osley, Sloan-Kettering Institute, Molecular Biology Program, Rockefeller Research Laboratory, Room 901E, 430 E. 67 Street, New York, NY. 10021, (212) 639-8156.

The Graduate Program in Molecular Biology brings together faculty members from a number of different departments who share common scientific interests.These departments include the Program in Molecular Biology of the Sloan-Kettering Institute and the Departments of Microbiology and of Cell Biology and Anatomy of Cornell University Medical College.This extended faculty provides the student with a broad spectrum of research opportunities and advanced courses.The Graduate Program in Molecular Biology prepares students for a career in basic research by providing them with both a strong academic background in molecular biology, genetics, and cell biology, and training as an experimentalist through laboratory rotations and thesis research.

Admission: A good background in genetics, molecular biology, chemistry, or biochemistry is required of students. Graduate Record Examination scores in both the aptitude test and an advanced test (Biology, Chemistry, or Biochemistry, Cell and Molecular Biology) are also required.

Course Requirements: Students complete a core sequence of Biochemistry, Graduate Biochemistry, Molecular Genetics, Eukaryotic Gene Structure and Function, and Journal Club Seminar during their first year. In addition, students participate in the Graduate Research Seminar Course throughout their enrollment.To complete the course requirements, four additional quarter equivalents of elective coursework are taken before graduation, chosen from a list of courses approved by the Curriculum Committee. This list currently includes: Nucleic Acids Enzymology, Advanced Cell Biology, Developmental Biology, Genetics, Molecular Virology, Molecular Biology of Growth Control and Neoplastic Transformation, Electron Microscopy, and Immunology.

All students, both PhD and MD-PhD, may petition the Curriculum Committee to exempt them from required or elective courses, if they can document taking

equivalent courses at other undergraduate or graduate institutions.

Laboratory Rotations: Students are required to rotate through three laboratories. Laboratory rotations begin immediately after a series of lectures by the faculty designed to familiarize students with the research underway in their laboratories. It is expected that students will have chosen their thesis mentors by the start of their second year in the program.

Admission to Doctoral Candidacy: The Admission to Doctoral Candidacy Examination (ACE) is administered in two sections: a written exam and an oral exam. For the written exam, the student prepares a research proposal on a topic selected by the student and approved by the ACE committee. The written proposal is reviewed by the ACE committee and returned to the student with a written critique. The oral exam tests a student's ability to respond to the comments in the critique as well as a student's general knowledge in the field of the proposal. This examination is given either in the Spring of the second year or the Fall of the third year.

Special Committee: A student's Special Committee will be chosen by the student in consultation with his/her mentor when the student selects a laboratory for thesis research. The function of the Special Committee is to evaluate the direction and progress of a student's thesis research and to provide an informational resource to the student.

Curriculum Committee: This committee, chaired by the Program Director and consisting of 8–10 members of the faculty, oversees all educational aspects of the program. The committee is responsible for assembling the curriculum, setting course requirements, adjudicating student applications for exemption from course requirements, and administering the evaluation of students at the end of their first year.

Academic Requirements for Students in the MD-PhD Program: MD-PhD students enter the Graduate Program following completion of (1) the Frontiers in Biomedical Science course, (2) two laboratory rotations during the summers preceding the first and second years of medical school, and (3) the first two years of the medical school curriculum, including Biochemistry and quarter II of Cell Biology and Microanatomy. The academic requirements for MD-PhD students are designed to prepare them for competitive careers in biomedical research in the interrelated fields of molecular biology, cell biology, and genetics. MD-PhD students initiate their thesis research during their third year; during this year they also complete four quarters of course work. The ACE is administered to MD-PhD students in the Fall of the fourth year. Starting in the Spring of their fourth year, they annually present a seminar on their thesis research in the Graduate Research Seminar Course.

Courses

Eukaryotic Gene Structure and Function. A semester-long course presenting the fundamentals of eukaryote gene structure, expression and regulation. Topics discussed include: DNA sequence organization, chromatin structure, viral and cellular RNA transcription, translation and its regulation, control of gene expression in model systems and molecular aspects of carcinogenesis. Third and fourth quarters, annually. Dr. Freedman and staff.

Nucleic Acids Enzymology. A formal course presenting the enzymological mechanisms and control of prokaryotic and eukaryotic transcription and DNA replication. Enzymes which alter DNA structure and shape are reviewed, and topics in DNA repair and recombination are also covered. Graduate Biochemistry is a prerequisite. First and second quarters, annually. Drs. Marians, Hurwitz, Holloman and O'Donnell.

Molecular Virology. A formal course in which major emphasis is placed on the basic mechanisms in the biology of all animal viruses, including RNA and DNA tumor viruses. The topics considered include virus structure and composition, assay of viruses and viral-specific products, transcription and replication of viral nucleic acids, translation of virus-specific proteins, assembly of viral particles, structural and functional alterations in viral-infected cells including transformation, pathogenesis of viral diseases, and viral genetics. Alternate years. Offered third and fourth quarters, 1994–95. Drs. Berns, Hayward, Besmer, Traktman, Lusky, and staff.

Molecular Genetics. This course, which is offered jointly with the Program in Cell Biology and Genetics, focuses on key topics of molecular genetics in bacteria and bacterial viruses, yeast, *Drosophila,* and mouse. The isolation of mutants and their analysis by recombination, complementation

and the generation of suppressors are discussed in depth. The course consists of lectures and interactive small-group discussion of research papers from the current literature. Limited to 36 students. Offered in 1993–94 as two sequential two-quarter courses with the first focusing on prokaryotic and simple eukaryotic systems, and the second covering complex eukaryotic systems and special topics. Quarters I and II: Drs. Ballinger, Caudy, Holloman, Lustig, Osley and Traktman. Quarters III and IV: Drs. Ballinger, Dorsett, Jasin, and Lacy.

Molecular Biology of Growth Control and Neoplastic Transformation. This course focuses on current efforts to understand the neoplastic cell phenotype from a molecular point of view. The effects of RNA and DNA tumor viruses on host cells are discussed, in particular the transformation and/or differentiation blocks of defined cell lineages by certain agents. The nature and enzymatic specificities of viral gene products responsible for transformation are compared with related products of normal cellular genes. The potential interaction of such products with regulatory systems controlling cell shape, adhesiveness, motility, and mitosis are described, as well as the possible involvement of the same systems in nonviral neoplasias. A section of the course is devoted to the molecular biology and biochemistry of cell surface growth factor- and polypeptide hormone-receptors and mechanisms of signal transmission across biological membranes. At least part of the course consists of student presentations on relevant subjects. Third and fourth quarters, alternate years. Offered in 1993–94. Drs. Hayward, Besmer, and Brown.

Graduate Research Seminar. This course represents an opportunity for all the faculty and students of the program to hear the upper-class students describe their research in formal seminar presentations. Quarters I–IV, annually. Dr. Lacy.

Journal Club Seminar for 1st Year Students. In this seminar, first-year students present and analyze scientific data. Each student presents two papers during the semester. Papers are chosen by the students and approved by the instructors. Speakers generally provide a brief relevant background and then present each figure in the paper summarizing the experimental method or assay used, the results illustrated, and the conclusions drawn. Participation by all students is encouraged during the presentation. Given jointly with the Program in Cell Biology and Genetics. Annually, quarters III and IV. Drs. Brown and Gumbiner.

Neuroscience

Graduate Program Chairman

Fred Plum, Department of Neurology and Neuroscience, Cornell University Medical College, Rm. A-569, 1300 York Avenue, New York, NY 10021, (212) 746-6575

Graduate Program Co-Directors

John A. Wagner, Department of Neurology and Neuroscience, Cornell University Medical College, Rm E-615A, 1300 York Avenue, New York, NY 10021, (212) 746-6586

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The Program in Neuroscience provides training in the study of the nervous system. It includes the disciplines of neuroanatomy, developmental neurobiology, neurophysiology, molecular biology, neurochemistry, molecular genetics, neuropharmacology and neuropsychology. The program emphasizes a multidisciplinary approach based on the belief that future advances in our understanding of the nervous system will be derived from the thinking and research techniques employed by more than one discipline. The program of research and course work for entering students is individualized. Students are expected to spend time working closely with members of the faculty whose research approach is complementary to their interests. In addition, there are regularly scheduled seminars during which various aspects of work in process are presented and discussed. By these means, students are afforded the broadest possible view of the neurosciences during their graduate training.

Admission: Applicants to the program are expected to have had thorough undergraduate training in biology, organic chemistry, physics, and mathematics. Many students enter this program after attaining an MD or a masters degree, and this is taken into consideration in formulating their training program. Graduate Record Examination

scores are to be submitted with the application. Candidates for admission are encouraged to visit the program.

Course Requirements for students in the PhD Program: Depending on prior background and needs, students will be expected to take a core sequence of courses during the first two years which includes introductory graduate courses in cell biology, molecular biology, and pharmacology, and the neuroscience program courses in molecular, biochemical, cellular, and systems neurobiology. Students will also select advanced graduate courses in the neurosciences and related fields to deepen their knowledge in areas of interest and develop a minor specialty. In addition, throughout their training, students are expected to participate in the weekly Progress-in-Neuroscience seminar series.

Course Requirements for students in the MD-PhD Program: Students in the MD-PhD program will enter the research intensive period of their training having completed both the first two years of the medical school curriculum and the Frontiers in Biomedical Science course. During the three years that these students spend in graduate studies, their major focus is laboratory research and preparation of papers and their thesis, but students are also expected to participate in research-oriented seminars. To prepare them for their research career, students are asked to take one upper-level course in the basic sciences and one upper-level course in the neurosciences, but this requirement depends on the preparation of the student. Generally, students in the program take the Admission to Candidacy Examination at the end of their third year.

Laboratory Rotations: These rotations allow students to experience research first-hand and acquaint themselves with the research faculty of the program. Students are expected to do two rotations of two quarters each but are welcome to do more before choosing their thesis advisor.

Admission to Doctoral Candidacy: Before the end of the second year, students will organize their Special Committee and take the qualifying exam. In the neurosciences, this exam is a combination of a tutorial-style review of selected subjects that are of interest to the student followed by a written exam and an oral defense of the student's research proposal.

Courses

Cellular Neuroscience. This course will cover fundamental concepts about nerve and glial cells including membrane potential and neurophysiology, structure of the neuron and its synapse, and developmental neurobiology. It is a prerequisite for the fourth quarter Neuroscience course. Second quarter, 1993-94. Dr. Townes-Anderson and the faculty of the Neuroscience program.

Neuroscience. This is an interdisciplinary course on the structure of the nervous system given jointly by the Department of Physiology and Biophysics and the Department of Cell Biology and Anatomy, with the participation of the Department of Neurology and Neuroscience. Includes lectures that correlate anatomical, physiological and clinical aspects of neuroscience, and computer-based teaching modules on neuroanatomy and neurophysiology, as well as patient presentations. Fourth quarter, annually. Drs. Brooks and Grafstein.

Molecular Basis of Neurological Disease. This course will review current attempts to understand neurological disease from a molecular point of view. Students will be taught the basic methods in molecular biology and molecular genetics and will learn how to apply these to the study of neurological disease. Second quarter, 1993-94, with adequate enrollment. Dr. Furneaux.

Neuropharmacology and Functional Neuroanatomy. This course is jointly sponsored by the Programs in Neuroscience and Pharmacology. It is designed to present current concepts of the major Central Nervous System (CNS) neurotransmitters and their functional neuroanatomy. The course will integrate discussions of the mechanisms of neurotransmitter biosynthesis and release, receptor signal transduction and the alterations produced by CNS drugs, with a description of how contemporary neuroanatomical methods are used to define neurotransmitter systems, their functions and interactions with drugs. Offered annually, third and fourth quarters. The course includes laboratory sessions. Course organizers: Drs. Milner, Inturrisi and Okamoto; Co-Instructors: Drs. Van Bockstaele and Aicher.

Research Proposals: Inspiration, Writing, and Evaluation. This seminar course will provide students with experience in developing and writing a research plan in an area of their own choosing, as well

as in critically evaluating the merits of specific approaches to scientific problems. Third quarter, 1993-94. Dr. Wagner and members of the graduate college.

Proseminar in Synaptic Physiology. The physiology and biophysics of synapses are explored by reading and discussion of seminal papers in the original literature. The first half of the course examines a model synapse, the mammalian neuromuscular junction, by intracellular recording, voltage clamping, noise analysis, and patch clamping. Topics in the second half include NMDA receptors, plasticity, and neural networks. Fourth quarter, 1993-94. Dr. Gardner.

Mathematical Structures in Neuroscience. The aim of this course is to provide a didactic introduction to a variety of mathematical structures. The structures are selected both because of their proven usefulness and their intrinsic interest. The emphasis will be on concepts, techniques and examples. Important theorems will be discussed but, in general, not proven. Rather, they will be illustrated through application and also through counter examples of would-be stronger theorems. First quarter, 1994-95, with adequate enrollment. Dr. Victor.

Behavioral Neuroscience. This course will cover the neural mechanisms of behavior. Current knowledge concerning the experimental analysis of a range of behaviors from developing and adult, invertebrate and vertebrate animals will be presented and discussed in 10 weekly sessions. The reciprocal interactions between brain and behavior will be emphasized. In addition to attending the lectures and participating in discussions, each student will be required to write a concise and critical review of a topic in Behavioral Neuroscience. First quarter, 1993-94. Drs. Smith and McEwen.

The Visual System. Lectures and readings on the functional organization of the vertebrate visual system at the molecular, cellular and systems levels. Topics will include phototransduction and signal processing within the retina, lateral geniculate nucleus and visual cortex. Third or fourth quarter, 1993-94. Drs. MacLeish and Victor.

Current Topics in Neurobiology. Discussion group format sessions, centered chiefly around upcoming lectures in the Program's weekly "Progress in Neuroscience" series. The speakers' recent primary papers and selected relevant reviews from leading journals will be used as text. Emphasis will be placed on critical evaluation of techniques and approaches as well as on provision of historical perspective and context, facilitating the students' appreciation of the work's significance. Second and third quarters, 1993-94, Dr. Sam Gandy and members of the program.

Introductory Biostatistics. This course covers descriptive statistics, normal distributions, comparison of groups, correlation, linear regression, and analysis of variance in biomedical research. Graphical presentation and use of computers will be emphasized. Second quarter, 1993-94. Dr. Greenberg.

Pharmacology

Graduate Program Co-Chairmen

Joseph R. Bertino, Sloan-Kettering Institute, Molecular Pharmacology and Therapeutics Program, Rockefeller Research Laboratories, Room 601, 1275 York Avenue, New York, NY 10021 (212) 639-8230

Lorraine J. Gudas, Department of Pharmacology, Cornell University Medical College, Room E-409, 1300 York Ave., New York, NY 10021, (212) 746-6250

Graduate Program Director

Charles E. Inturrisi, Department of Pharmacology, Cornell University Medical College, Room LC-524, 1300 York Ave., New York, NY 10021, (212) 746-6235

The Program in Pharmacology brings together faculty members from the Department of Pharmacology, Cornell University Medical College and the Program of Molecular Pharmacology and Therapeutics of the Sloan-Kettering Institute for Cancer Research. This interdisciplinary faculty provides the student with a broad spectrum of research opportunities and advanced courses in pharmacology.

Admission: A baccalaureate degree with a strong background in the natural sciences and/or health sciences is required for admission. Results of the Graduate Record Examination (verbal, quantitative and analytical) are required for PhD applicants, while the results of the advanced test in Biology or Chemistry will be considered. For applications to the MD-PhD program, the

results of the Medical College Admission Test are accepted in lieu of the Graduate Record Examination.

Course Requirements: In the first two years, students are expected to complete a core curriculum that may include the following courses: Introduction to Pharmacological Principles, Biochemistry, Biostatistics, Physiology and Biophysics, General Pharmacology, Molecular Pharmacology, Neuropharmacology and Functional Neuroanatomy and Pharmacology Research Seminar. Each student also completes two electives by June of the second year. These electives are selected from courses that are offered by other programs at the graduate school. Recent choices include: Graduate Biochemistry, Advanced Cell Biology, Neuroscience, and Eukaryotic Gene Structure and Function.

Program Supervision and Laboratory Rotations: The Program Director and the Curriculum Committee will supervise the student's graduate program until the student selects a faculty member to serve as the major sponsor. Three laboratory rotations are required of each student. These rotations provide the opportunity for the student to participate in the diverse research activities that are available within the Program. This experience is designed to assist the student in the selection of major and minor sponsors for the thesis research.

Admission to Doctoral Candidacy: The Admission to Candidacy Examination consists of two parts: a uniform written exam and an oral exam which includes discussion of a written research proposal. It is expected that most students will take this exam by the end of May of their second year.

Special Committee: The Special Committee includes a major faculty sponsor and two minor faculty sponsors. The Program Director will assist the student in the selection of the major (thesis) advisor.

Courses

Introduction to Pharmacological Principles. This course is designed to introduce the student to concepts unique to pharmacology. The introductory course will emphasize general concepts in receptor theory, the dose-response relationship, mechanisms of drug action and resistance, pharmacokinetics, metabolism, tolerance and dependence. All first-year graduate students in pharmacology are required to take this course, which is also open to all students in the graduate school. First quarter, annually. Dr. Pasternak and staff.

General Pharmacology. This basic pharmacology course consists of lectures, demonstrations, and small-group conferences. The purpose of these exercises is to teach the principles of pharmacology to second-year medical students and to graduate students. Detailed consideration is given to the parameters of drug action to provide the student with the fundamental concepts essential for evaluation of any drug. Consequently, the scientific basis of pharmacology is emphasized. Prototype drugs, essentially considered systemically, serve to illustrate several mechanisms and parameters of drug action. Therapeutic applications are considered insofar as they illustrate principles of pharmacology or drug hazards. Second and third quarters, annually. Dr. Chan and staff.

Neuropharmacology and Functional Neuroanatomy. This course is jointly sponsored by the Programs in Neuroscience and Pharmacology. It is designed to present current concepts of the major Central Nervous System (CNS) neurotransmitters and their functional neuroanatomy. The course will integrate discussions of the mechanisms of neurotransmitter biosynthesis and release, receptor signal transduction and the alterations produced by CNS drugs, with a description of how contemporary neuroanatomical methods are used to define neurotransmitter systems, their functions and interactions with drugs. The course includes laboratory sessions. Offered annually third and fourth quarters. Course organizers: Drs. Milner, Inturrisi and Okamoto. Co-Instructors: Drs. Van Bockstaele and Aicher.

Molecular Pharmacology. This course examines drug action at the molecular level. Topics include: interaction of drugs with macromolecules, drug resistance, membrane transport, regulation of gene expression, gene transfer, novel mechanisms of drug delivery, antiviral agents, antisense and monoclonal antibody therapy. Offered 1994–95, fourth quarter. Dr. Bertino, Dr. Scotto, and staff.

Pharmacology Research Seminar. Topics of contemporary pharmacological interest and new concepts and methodological approaches in biological research will be presented by guest speakers, faculty members or students. The presentations are followed by a discussion session which provides an opportunity for students to meet and talk to leading scientists in the field.

Details of events will be announced in advance. Third and fourth quarters, 1993–1994. Dr. Szeto.

Other Academic Offerings

Research in Pharmacology. Research opportunities may be arranged throughout the year for graduate students who are not majoring in pharmacology but who want some investigative experience in the discipline. Special opportunities are offered for work on the nervous and cardiovascular systems and in biochemical and clinical aspects of pharmacology.

Journal Club. This course is designed to improve graduate students' skills in public presentation. On a rotating basis, students prepare an oral presentation on a topic of their choice. The presentation is informally critiqued by the faculty. First through fourth quarters, annually; see the Program Director for further information.

Physiology and Biophysics

Graduate Program Chairman

Erich E. Windhager, Department of Physiology and Biophysics, Cornell University Medical College, Room C-508, 1300 York Avenue, New York, NY 10021, (212) 746-6358

Graduate Program Director

Olaf S. Andersen, Department of Physiology and Biophysics, Cornell University Medical College, Room LC-501, 1300 York Avenue, New York, NY 10021, (212) 746-6350

Opportunities are offered toward the PhD degree in several areas of physiology aid biophysics. Ample space is available, and laboratories are well equipped to provide predoctoral training in a medical environment. Interested individuals are urged to contact the Program Director before preparing a formal application. Letters of inquiry should include a discussion of the educational background and indicate possible areas of emphasis in graduate study. There has been a tendency to encourage applications from individuals who have a probable interest in more than one of the areas of physiology represented within the program.

Applicants must have completed courses in biology, inorganic and organic chemistry, physics, and mathematics through the level of differential and integral calculus. Additional course work in these disciplines at the undergraduate level is encouraged. Graduate Record Examination are required and advanced subject tests are recommended. Applicants whose native language is not English are, in addition, required to take the TOEFL. Applicants with otherwise exemplary records who lack certain course requirements will be considered for acceptance provided that they remedy their deficiencies while in training.

Course Requirements: The course of study emphasizes the importance of teaching and research in the preparation and development of individuals for careers in physiology. This goal is achieved by a combination of didactic courses, seminars, and closely supervised research leading toward the preparation of a satisfactory thesis.

A special program of study will be developed for each student in consultation with his or her Special Committee. (For MD-PhD students the program will take into consideration their coursework during the first two medical school years.)

1. In the first two years, students are expected to complete a course curriculum that may include: biochemistry, cell biology, molecular biology and genetics, neuroscience, pharmacology, and physiology and biophysics.
2. In addition, students will, during the first two years, have two or three laboratory rotations of about three months duration. A thesis advisor is chosen by the summer of the first year, and a Special Committee consisting of this major research advisor and two minor advisors is constituted to guide the student in research preparation. Students start thesis research before completing formal course-work, but they are not admitted to PhD candidacy before passing the Admission to Doctoral Candidacy Examination towards the end of the second year or early in the third year.

Courses

Physiology and Biophysics. Lectures and conferences on body fluid, bioelectric phenomena, endocrinology and circulation. Third quarter, annually. Dr. Windhager and staff.

Endocrinology is taught as an interdisciplinary course during two weeks of this quarter using hours normally allocated not only to courses in physiology, but also in cell

biology, and biochemistry (course coordinator: Dr. Greif).

Lectures and conferences on respiration, kidney function, acid-base regulation, and gastrointestinal function; and a weekly laboratory on selected aspects of physiology. Fourth quarter, annually. Dr. Windhager and staff.

Neuroscience. An interdisciplinary course on the structure and function of the human nervous system given jointly by the Department of Physiology and Biophysics and the Department of Cell Biology and Anatomy, with the participation of the Department of Neurology and Neuroscience. Includes lectures that correlate anatomical, physiological and clinical aspects of neuroscience, and computer-based teaching modules on neuroanatomy and neurophysiology, as well as patient presentations. Fourth quarter annually. Organized by Drs. Grafstein and Brooks.

Topics in Membrane Physiology. This weekly 2-hour conference is designed for PhD and MD-PhD students with a major or minor in Physiology and Biophysics. It is at a somewhat advanced level, especially in its quantitative approach to physiology. The aims of the conference are to train students in physiological concepts, to facilitate the understanding of lecture material in the Physiology and Biophysics course, and to establish close student-faculty contact. Third quarter, annually. Dr. Andersen.

Ionic Channels. The course covers mathematical and experimental approaches to the topic of ion movement through single channels. Minimum of 5 students. Prerequisite: 2 years of calculus. Fourth quarter, annually. Dr. Andersen and invited lecturers.

Mathematical Models of Membrane Transport. The general, thermodynamic description of membrane and epithelial transport will be reviewed (with reference to Katchalsky, Curran and Schultz, Sauer, Essig and Caplan). Comparison with kinetic descriptions of membrane transport will be considered (Heinz, Hill). The analysis of composite membrane systems will be examined (Kedem and Katchalsky) as a prelude to the construction of epithelial simulations (Sackin and Boulpaep, Weinstein and Stephenson). Examples of such simulations will be used to examine transport along the kidney tubule under normal and pathological conditions. Third and fourth quarter, annually. Dr. Weinstein.

Selected Topics in Kidney and Electrolyte Physiology and Pathophysiology. Lectures, seminars and demonstrations. Topics include: (1) GFR, clearance concept, reabsorption and secretion of electrolytes; (2) concentrating mechanism; (3) electrophysiology of the nephron; (4) pathophysiology of potassium; (5) renal hemodynamics; (6) control of body fluid volume and tonicity; (7) control of acid base balance; (8) pathology and pathophysiology of renal failure. Minimum of 8 students. Fourth quarter, annually. Drs. Maack, Windhager, and staff.

Topics in Gastrointestinal Physiology. Lectures and Seminars. Topics include: (1) functional morphology of stomach and intestine; (2) proliferation and differentiation of gastrointestinal cells; (3) motility of esophagus, small intestine and colon; (4) gastric and intestinal secretion; pancreatic secretion; (5) lipid absorption; (6) intestinal absorption of calcium and vitamin D; (7) structure and function of bile acids; (8) gastrointestinal hormones. Minimum: 8 students. Fourth quarter, annually. Dr. Lipkin and invited experts in the field.

Biophysics for Biologists. See description under Cell Biology and Genetics. Fourth quarter, annually. Drs. Andersen, Breslow, Pardee, Roepe, and Scotto.

Proseminar in Synaptic Physiology. See description under Neuroscience. Fourth quarter, annually. Dr. Gardner.

Cellular Neuroscience. See description under Neuroscience. Third quarter, annually. Dr. Townes-Anderson.

MD-PhD Program

Requirements for the PhD component of the MD-PhD Program are satisfied by completion of the first two years of the Medical College curriculum including the *Frontiers of Biomedical Science* course and 1 to 3 additional courses to be determined by the student's chosen Program of Study, with consideration of the prior experience of the student. During the first two summers the student is expected to complete laboratory rotation requirements. The tutorial-based Admission-to-Doctoral-Candidacy Examination will assist the student in developing a research thesis project.

Register

University Administration

Frank H. T. Rhodes, President

Malden C. Nesheim, Provost

Robert Michels, Provost for Medical Affairs and Dean of the Medical College

James E. Morley, Jr., Senior Vice President

Joyce W. Cima, Acting Secretary of the Corporation

Michael G. Kimberly, Acting University Counsel

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Graduate School of Medical Sciences

Administration

Frank H. T. Rhodes, President of the University

Alison P. Casarett, Dean of the Graduate School

Donald A. Fischman, Dean of the Graduate School of Medical Sciences, Associate Dean of the Graduate School

Dieter H. Sussdorf, Associate Dean of the Graduate School of Medical Sciences, Assistant Dean of the Graduate School

Richard A. Rifkind, Director, Sloan-Kettering Division

Jerard Hurwitz, Director of Graduate Studies, Sloan-Kettering Division

Standing Committees

Executive Committee

Donald A. Fischman, Chair

Kenneth I. Berns

Joseph R. Bertino

Esther M. Breslow

George Brown*

Lorraine J. Gudas

Jerard Hurwitz

Kenneth O. Lloyd

Kenneth J. Marians

Joan Massagué

Robert Michels

Mary Ann Osley

Fred Plum

Enrique Rodriguez-Boulan

Peter J. Romanienko*

Kendall A. Smith

Dieter H. Sussdorf

John A. Wagner

Erich E. Windhager

Faculty Advisory Committee

John A. Wagner, Chair

Olaf S. Andersen

David M. Bader

Donald A. Fischman*

Kathleen Guger

David P. Hajjar

Jerard Hurwitz*

Charles E. Inturissi

Janet S. Lee

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Clarissa Naftzger

Mary Ann Osley

Gavril N. Pasternak

Dieter H. Sussdorf*

Graduate Student Executive Council

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Heshani de Silva

David A. Egan

Kathleen Guger

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Clarissa Naftzger

Peter J. Romanienko

Cindy Taylor

Michelle Tourigny

Jason Tsai

Tonya Villafana

Graduate Student/Faculty Liaison Committee

Jason Tsai, Chair

David A. Circle

David A. Egan

Donald A. Fischman*

Kenneth J. Marians

Joel D. Pardee

Dieter H. Sussdorf*

Tonya Villafana

**nonvoting member*

Faculty

Albino, Anthony P., Assistant Professor of Immunology. B.A. 1970, Hunter College of the City University of New York; Ph.D. 1974, Cornell University

Alonso, Daniel R., Professor of Pathology. M.D. 1962, University of Cuyo (Argentina)

Andersen, Olaf S., Professor of Physiology and Biophysics. Candidatus Medicinae 1971, University of Copenhagen (Denmark)

Anderson, Mary E., Assistant Professor of Biochemistry. B.A. 1977, Hollins College; Ph.D. 1983, Cornell University Graduate School of Medical Sciences

Bachvarova, Rosemary F., Professor of Cell Biology and Anatomy. B.A. 1961, Radcliffe College; Ph.D. 1966, The Rockefeller University

Bader, David M., Associate Professor of Cell Biology and Anatomy. B.A. 1974, Augustana College; Ph.D. 1978, University of North Dakota

Baker, Harriet D., Associate Research Professor of Neuroscience. B.A. 1963, Wells College; M.S. 1967, University of Illinois; Ph.D. 1976, University of Iowa

Ballinger, Dennis G., Assistant Professor of Molecular Biology. B.A. 1978, University of Colorado; Ph.D. 1984, Massachusetts Institute of Technology

Barany, Francis, Associate Professor of Microbiology. B.A. 1976, University of Illinois at Chicago Circle; Ph.D. 1981, The Rockefeller University

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Berns, Kenneth I., The R.A. Rees Pritchett Professor of Microbiology, Professor of Microbiology in Pediatrics. A.B. 1960, Ph.D. 1964, M.D. 1966, Johns Hopkins University

Bertino, Joseph R., American Cancer Society Research Professor, Professor of Molecular Pharmacology and Therapeutics. Professor of Medicine. Professor of Pharmacology. B.S. 1950, Cornell University; M.D. 1954, Downstate Medical Center

Besmer, Peter, Professor of Molecular Biology. M.S. 1964; Ph.D. 1969, Eidgenoessische Technische Hochschule (Switzerland)

Biedler, June L., Professor of Cell Biology and Genetics. A.B. 1947, Vassar College; Ph.D. 1959, Cornell University

Black, Ira B., Adjunct Professor of Neurology and Neuroscience (Robert Wood Johnson Medical School). A.B. 1961, Columbia College; M.D. 1965, Harvard University

Blanck, Thomas J. J., Professor of Anesthesiology. B.S. 1966, Yale University; M.D. 1970, Ph.D. 1974, University of Pennsylvania

Blasberg, Ronald G., Professor of Neurology. B.A. 1961, Colgate University; M.D. 1967, Albert Einstein College of Medicine

Blass, John P., The Winifred Masterson Burke Professor of Neurology. Professor of Medicine. A.B. 1958, Harvard University; Ph.D. 1960, University of London (United Kingdom); M.D. 1965, Columbia University

Blobel, Carl Peter, Assistant Professor of Cell Biology and Genetics. M.D. 1984, Justus Liebig University (Germany); Ph.D. 1991, University of California, San Francisco

Boskey, Adele L., Professor of Biochemistry. B.A. 1964, Barnard College; Ph.D. 1970, Boston University

Bovbjerg, Dana H., Assistant Professor of Immunology. Assistant Professor of Immunology in Neuroscience. B.A. 1973, Carleton College; B.S. 1977, University of Iowa; Ph.D. 1983, University of Rochester School of Medicine and Dentistry

Breslow, Esther M., Professor of Biochemistry. B.S. 1953, Cornell University; M.S. 1955, Ph.D. 1959, New York University

Brooks, Dana C., Professor of Cell Biology and Anatomy. B.E.E. 1949, M.D. 1957, Cornell University Medical College

Brown, Anthony M. C., Associate Professor of Cell Biology and Anatomy. Assistant Professor of Cell Biology and Anatomy in Microbiology. B.A. 1977, M.A. 1979, University of Cambridge (United Kingdom); Ph.D. 1981, University of Edinburgh (United Kingdom)

Buck, Jochen, Assistant Professor of Pharmacology. M.D. 1984, Ph.D. 1985, University of Tübingen (Germany)

Bullough, Peter, Professor of Pathology. M.D. 1956, Liverpool University (United Kingdom)

Caudy, Michael, Assistant Professor of Cell Biology and Anatomy. Ph.D. 1985, University of California, Berkeley

Chaganti, Raju S., Professor of Cell Biology and Genetics. Professor of Genetics in Pathology. B.S. 1954, M.S. 1955, Andhra University (India); Ph.D. 1964, Harvard University

Chan, Walter W. Y., Professor of Pharmacology. B.A. 1956, University of Wisconsin; Ph.D. 1961, Columbia University

Chao, Moses V., Professor of Cell Biology and Anatomy. Professor of Cell Biology and Anatomy in Medicine. B.A. 1973, Pomona College; Ph.D. 1980, University of California at Los Angeles

Chiorazzi, Nicholas, Professor of Medicine. B.A. 1966, College of the Holy Cross; M.D. 1970, Georgetown University School of Medicine

Chou, Ting-Chao, Professor of Molecular Pharmacology and Therapeutics. B.S. 1961, Kaohsiung Medical College (Republic of China); M.S. 1965, National Taiwan University (Republic of China); Ph.D. 1970, Yale University

Citi, Sandra, Assistant Professor of Cell Biology and Anatomy. M.D. 1989, University of Florence (Italy); Ph.D. 1986, Cambridge University (United Kingdom)

Cohen, Jacques, Associate Professor of Embryology in Obstetrics and Gynecology. B.Sc. 1974, State University of Leiden (The Netherlands); M.Sc. 1978, Ph.D. 1982, Erasmus University (The Netherlands)

Cooper, Arthur J. L., Research Professor of Biochemistry. Research Professor of Biochemistry in Neuroscience. B.Sc. 1967, M.Sc. 1969, University of London (United Kingdom); Ph.D. 1974, Cornell University Graduate School of Medical Sciences

Crow, Mary Kuntz, Associate Professor of Medicine. B.A. 1972, Manhattanville College; M.D. 1978, Cornell University Medical College

DeLotto, Robert, Assistant Professor of Molecular Biology. B.A. 1976, University of Pennsylvania; Ph.D. 1983, Princeton University

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Duvoisin, Robert, Assistant Professor of Cell Biology in Ophthalmology, B.Sc. 1979, Ph.D. 1987, University of Geneva (Switzerland)

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Elkon, Keith B., Associate Professor of Medicine. M.D. 1974, University of the Witwatersrand Medical School (South Africa)

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Fairclough, Gordon F., Associate Professor of Clinical Biochemistry. Associate Professor of Clinical Biochemistry in Pathology. B.A. 1960, Ph.D. 1966, Yale University

Falck-Pedersen, Erik, Associate Professor of Microbiology. B.A. 1976, North Central College; Ph.D. 1982, University of Illinois

Felsen, Diane D., Associate Research Professor of Pharmacology in Surgery. B.A. 1974, Queens College of the City University of New York; Ph.D. 1979, Mount Sinai School of Medicine

Fischman, Donald A., Dean, The Harvey Klein Professor of Biomedical Sciences. Professor of Cell Biology and Anatomy. A.B. 1957, Kenyon College; M.D. 1961, Cornell University Medical College

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Friedman, Steven Michael, Associate Professor of Medicine. B.A. 1968, Princeton University; M.D. 1972, Cornell University Medical College

Furneaux, Henry M., Assistant Professor of Molecular Pharmacology and Therapeutics. Assistant Professor of Molecular Biology in Neuroscience. B.Sc. 1975, Ph.D. 1978, University of Aberdeen (United Kingdom)

Gandy, Samuel, Assistant Professor of Neurology and Neuroscience. B.S. 1976, Charleston Southern University; M.D., Ph.D. 1982, Medical University of South Carolina

Gardner, Daniel, Professor of Physiology and Biophysics. Professor of Physiology and Biophysics in Neuroscience. A.B. 1966, Columbia College; Ph.D. 1971, New York University

German, James L. III, Clinical Professor of Pediatrics. B.S. 1945, Louisiana Polytechnic Institute; M.D. 1949, Southwestern Medical College

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Gibbs, James G. Jr., Professor of Psychiatry. B.S. 1960, Trinity College; M.D. 1964, Medical College of South Carolina

Gibson, Gary E., Professor of Neuroscience. B.S. 1968, University of Wyoming; Ph.D. 1973, Cornell University

Gilboa, Eli, Adjunct Associate Professor of Molecular Biology. B.Sc. 1971, M.Sc. 1973, The Hebrew University of Jerusalem (Israel); Ph.D. 1977, Weizmann Institute of Science (Israel)

Golde, David W., Enid A. Haupt Professor of Hematologic Ocology, Professor of Molecular Pharmacology and Therapeutics, Professor of Medicine. B. S. 1962, Fairleigh Dickinson University; M. D., C. M. 1966, McGill University (Canada)

Goldman, Steven A., Associate Professor of Neurology and Neuroscience. B.A. 1978, University of Pennsylvania; M.D. 1984, Cornell University Medical College; Ph.D. 1983, The Rockefeller University

Goldstein, Jack, Adjunct Associate Professor of Biochemistry. B.A. 1952, Brooklyn College of the City University of New York; M.N.S. 1957, Ph.D. 1959, Cornell University

Grafstein, Bernice, The Vincent and Brooke Astor Distinguished Professor in Neuroscience. Professor of Physiology and Biophysics. B.A. 1951, University of Toronto (Canada); Ph.D. 1954, McGill University (Canada)

Greenberg, Danielle, Assistant Professor of Psychology in Psychiatry. B.S. 1975, Columbia University; M.Phil. 1983, Ph.D. 1984, City College of the City University of New York

Greif, Roger L., Professor Emeritus of Physiology and Biophysics. B.S. 1937, Haverford College; M.D. 1941, Johns Hopkins University

Gross, Steven S., Assistant Professor of Pharmacology. B.S. 1974, Brooklyn College of the City University of New York; M.P.H. 1979, Ph.D. 1982, Mount Sinai School of Medicine

Gudas, Lorraine J., The Revlon Pharmaceutical Professor of Pharmacology and Toxicology. Professor of Pharmacology. B.A. 1970, Smith College; Ph.D. 1975, Princeton University

Gumbiner, Barry M., Associate Professor of Cell Biology and Genetics. B.S. 1976, University of Cincinnati; Ph.D. 1982, University of California, San Francisco

Hackett, Neil R., Assistant Professor of Microbiology. B.Sc. 1978, University of Edinburgh (United Kingdom); Ph.D. 1982, University of British Columbia (Canada)

Hajjar, David P., Professor of Pathology. Professor of Biochemistry. B.A. 1974, American International College; M.S. 1977, Ph.D. 1978, University of New Hampshire

Hajjar, Katherine A., Associate Professor of Pediatrics. Associate Professor of Pediatrics in Medicine. A.B. 1974, Smith College; M.D. 1978, Johns Hopkins University School of Medicine

Hämmerling, Ulrich, Professor of Immunology. Diplom 1961 Universität Freiburg (Germany); Ph.D. 1965, Max Planck Institut für Immunobiologie (Germany)

Hartl, Franz-Ulrich, Professor of Cell Biology and Genetics. M.D. 1985, University of Heidelberg (Germany)

Haschemeyer, Rudy H., Professor of Biochemistry. B.A. 1952, Carthage College; Ph.D. 1957, University of Illinois

Hayward, William S., Professor of Molecular Biology. B.A. 1964, University of California, Riverside; Ph.D. 1969, University of California, San Diego

Hemmings, Hugh Carroll, Jr., Assistant Professor of Anesthesiology, Assistant Professor of Pharmacology. B.S. 1978, Ph.D. 1986, Yale University; M.D. 1987, Yale University School of Medicine

Hirsch, Joy, Professor of Molecular Pharmacology and Therapeutics, Professor of Neuroscience. B.S. 1969, University of Oregon; M.S. 1971, Portland State University; Ph.D. 1977, Columbia University

Holloman, William K., Professor of Microbiology. B.S. 1967, University of Texas: Ph.D. 1971, University of California, Berkeley

Horecker, Bernard L., Professor Emeritus of Biochemistry. B.S. 1936, Ph.D. 1939, University of Chicago

Houghton, Alan N., Professor of Immunology. Professor of Medicine. B.A. 1970, Stanford University; M.D. 1974, University of Connecticut

Hurwitz, Jerard, American Cancer Society Research Professor. Professor of Molecular Biology. B.A. 1949, Indiana University; Ph.D. 1953, Western Reserve University

Hutchison, Dorris J., Professor Emeritus of Cell Biology and Genetics. B.S. 1940, Western Kentucky State College; M.S. 1943, University of Kentucky; Ph.D. 1949, Rutgers University

Inturrisi, Charles E., Professor of Pharmacology. B.S. 1962, University of Connecticut; M.S. 1965, Ph.D. 1967, Tulane University

Jaffe, Eric, Professor of Medicine. M.D. 1966, State University of New York, Downstate Medical Center

Jasin, Maria, Assistant Professor of Cell Biology and Genetics. B.S. 1978, Florida Atlantic University; Ph.D. 1984, Massachusetts Institute of Technology

Joh, Tong Hyub, Professor of Neuroscience. B.S. 1953, Seoul National University (Korea); Ph.D. 1971, New York University

Kimberly, Robert Parker, Professor of Medicine. A.B. 1968, Princeton University; B.A., M.A. 1970, Oxford University (United Kingdom); M.D. 1973, Harvard Medical School

Klein, Irwin L., Professor of Medicine. B.A. 1969, University of Pennsylvania; M.D. 1973, New York University School of Medicine

Koutcher, Jason A., Associate Professor of Physics in Radiology. B.S. 1972, Massachusetts Institute of Technology; M.D., Ph.D. 1979, State University of New York Health Science Center at Brooklyn

Lacy, Elizabeth, Associate Professor of Molecular Biology. B.A. 1974, University of Pennsylvania; Ph.D. 1980, California Institute of Technology

Lai, Eseng, Assistant Professor of Cell Biology and Genetics. B.A. 1977, Yale University; M.D., Ph.D. 1983, Albert Einstein College of Medicine

Laughlin, John S., Professor of Molecular Pharmacology and Therapeutics. A.B. 1940, Willamette University; Ph.D. 1947, University of Illinois

Lee, Janet S., Associate Professor of Immunology. B.A. 1972, University of Minnesota; M.S. 1974, University of Wisconsin; Ph.D. 1979, University of California at San Francisco

Levi, Roberto, Professor of Pharmacology. M.D. 1960, University of Florence (Italy)

Li, Gloria C., Professor of Biophysics in Radiology. B.S. 1963, National Taiwan University (Republic of China); M.S. 1966, University of Houston; Ph.D. 1971, Stanford University

Ling, C. Clifton, Professor of Molecular Pharmacology and Therapeutics. Professor of Physiology in Radiology. B.S. 1965, Oregon State University; Ph.D. 1971, University of Washington

Lipkin, Martin, Professor of Medicine. A.B. 1946, M.D. 1950, New York University

Lloyd, Kenneth O., Professor of Immunology. Ph.D. 1960, University of College of North Wales (United Kingdom)

Lusky, Monika, Assistant Professor of Microbiology. B.A. 1973, M.A. 1975, M.S. 1977, Ph.D. 1980, Albert-Ludwigs University, Freiburg (Germany)

Lustig, Arthur J., Assistant Professor of Molecular Biology. B.A. 1975, Ph.D. 1981, The University of Chicago

Maack, Thomas, Professor of Physiology and Biophysics. M.D. 1962, University of São Paulo (Brazil)

MacLeish, Peter R., Professor of Physiology in Ophthalmology. Professor of Physiology and Biophysics. B.E.Sc. 1969, University of Western Ontario (Canada); Ph.D. 1976, Harvard University

Marians, Kenneth J., Professor of Molecular Biology. B.S. 1972, Polytechnic Institute of Brooklyn; Ph.D. 1976, Cornell University

Marks, Paul A., Professor of Cell Biology and Genetics. Professor of Medicine. A.B. 1945, Columbia University; M.D. 1949, College of Physicians and Surgeons, Columbia University

Massagué, Joan, Howard Hughes Medical Institute Investigator. Professor of Cell Biology and Genetics. Licenciado en Farmacia 1975, Graduado en Farmacia 1975, Doctor en Farmacia 1978, University of Barcelona (Spain)

Meister, Alton, The Israel Rogosin Professor Emeritus of Biochemistry. B.S. 1942, Harvard University; M.D. 1945, Cornell University Medical College

Mendelsohn, John, Professor of Molecular Pharmacology and Therapeutics. Professor of Medicine. B.A. 1958, Harvard College; M.D. 1963, Harvard Medical College

Mikawa, Takashi, Assistant Professor of Cell Biology and Anatomy. B.Sc. 1975, Kobe University (Japan); M.S. 1977, Ph.D. 1980, Kyoto University (Japan)

Milner, Teresa A., Assistant Professor of Neuroscience. B.S. 1978, University of California, Irvine; Ph.D. 1982, University of California, San Diego

Minick, C. Richard, Professor of Pathology. B.S. 1957, University of Wyoming; M.D. 1960, Cornell University Medical College

Moore, Malcolm A.S., Professor of Cell Biology and Genetics. M.B. 1963, B.A. 1964, D.Phil. 1967, M.A. 1970, Oxford University (United Kingdom)

Muller-Eberhard, Ursula, Professor of Pediatrics. Professor of Pharmacology. M.D. 1953, University of Göttingen (Germany)

Murray, Henry W., Professor of Medicine, B.A. 1968, Cornell University; M.D. 1972, Cornell University Medical College

Nachman, Ralph L., The Mark W. Pasmantier Professor of Medicine. A.B. 1953, M.D. 1956, Vanderbilt University

Nathan, Carl F., The Stanton Griffis Distinguished Professor of Medicine. B.A. 1967, Harvard University; M.D. 1972, Harvard Medical School

Nikolic-Zugic, Janko, Assistant Professor of Immunology, M.D. 1984, Ph.D. 1993, Belgrade University Medical School (Yugoslavia)

Novogrodsky, Abraham, Professor of Biochemistry. Professor of Biochemistry in Medicine. M.D. 1960, Hebrew University Medical School, Jerusalem (Israel); Ph.D. 1974, Weizmann Institute of Science (Israel)

O'Donnell, Michael E., Associate Professor of Microbiology. B.S. 1975, University of Portland; Ph.D. 1982, University of Michigan

Okamoto, Michiko, Professor of Pharmacology. Professor of Pharmacology in Anesthesiology. B.S. 1954, Tokyo College of Pharmacy (Japan); M.S. 1957, Purdue University; Ph.D. 1964, Cornell University Graduate School of Medical Sciences

Old, Lloyd J., Professor of Immunology. B.A. 1955, M.D. 1958, University of California

O'Leary, William M., Professor of Microbiology. B.S. 1952, M.S. 1953, Ph.D. 1957, University of Pittsburgh

O'Reilly, Richard J., Professor of Immunology. Professor of Pediatrics. A.B. 1964, College of the Holy Cross; M.D. 1968, University of Rochester

Osley, Mary Ann, Associate Professor of Molecular Biology. B.A. 1967, Wheaton College; Ph.D. 1973, Yale University

Palmer, Lawrence G., Professor of Physiology and Biophysics. B.A. 1970, Swarthmore College; Ph.D. 1976, University of Pennsylvania

Pardee, Joel D., Associate Professor of Cell Biology and Anatomy. B.S. 1973, Colorado State University; Ph.D. 1978, Stanford University

Pasternak, Gavril W., Professor of Molecular Pharmacology and Therapeutics. Professor of Pharmacology. Professor of Neurology and Neuroscience. B.A. 1969, M.D. 1973, Ph.D. 1974, Johns Hopkins University

Pickel, Virginia M., Professor of Neuroscience. B.S. 1965, M.S. 1967, University of Tennessee; Ph.D. 1970, Vanderbilt University

Plum, Fred, The Anne Parrish Titzell Professor of Neurology. B.A. 1944, Dartmouth College; M.D. 1947, Cornell University Medical College

Posner, Jerome B., Professor of Molecular Pharmacology and Therapeutics. Professor of Neurology and Neuroscience. B.S. 1951, University of Washington; M.D. 1955, University of Washington School of Medicine

Posnett, David Neil, Associate Professor of Medicine. M.D. 1977, University of Geneva (Switzerland)

Prince, Alfred M., Clinical Associate Professor of Pathology. A.B. 1949, Yale University; M.A. 1951, Columbia University; M.D. 1955, Western Reserve University

Prochaska, Hans J., Assistant Professor of Molecular Pharmacology and Therapeutics. B.S.Ch.E. 1981, Rutgers University; M.D., Ph.D. 1986, Johns Hopkins University School of Medicine

Pulsinelli, William Anthony, Adjunct Professor of Neurology and Neuroscience. B.S. 1965, Villanova University; Ph.D. 1970, M.D. 1973, University of Utah College of Medicine

Quimby, Fred, Associate Professor of Pathology. V.D.M. 1970, University of Pennsylvania School of Veterinary Medicine; Ph.D. 1974, University of Pennsylvania Graduate School of Arts and Sciences

Ravetch, Jeffrey A., Professor of Molecular Biology. B.S. 1973, Yale University; Ph.D. 1978, The Rockefeller University; M.D. 1979, Cornell University Medical College

Rayson, Barbara, Associate Research Professor of Physiology and Biophysics; B.Sc. 1972, Ph.D. 1976, University of Melbourne (Australia)

Reidenberg, Marcus M., Professor of Pharmacology. Professor of Medicine. M.D. 1958, Temple University School of Medicine

Reis, Donald J., The George C. Cotzias Distinguished Professor of Neurology. Professor of Neurology in Psychiatry. A.B. 1953, M.D. 1956, Cornell University Medical College

Resh, Marilyn D., Associate Professor of Cell Biology and Genetics. B.A. 1977, Princeton University; Ph.D. 1982, Harvard University

Rettig, Wolfgang, Assistant Professor of Immunology. M.D. 1979, Ph.D. 1983, Freie Universität Berlin (Germany)

Rifkind, Arleen B., Professor of Pharmacology; Associate Professor of Medicine. B.A. 1960, Bryn Mawr College; M.D. 1964, New York University

Rifkind, Richard A., Director, Sloan-Kettering Division, Professor of Cell Biology and Genetics. B.S. 1951, Yale University; M.D. 1955, Columbia University

Riker, Walter F., Jr., The Revlon Pharmaceutical Professor Emeritus of Pharmacology and Toxicology. Professor Emeritus of Pharmacology. B.S. 1939, Columbia University; M.D. 1943, Cornell University Medical College

Robertson, Hugh D., Associate Professor of Biochemistry. B.A. 1964, Harvard College; Ph.D. 1969, The Rockefeller University

Rodriguez-Boulan, Enrique, The Joseph C. Hinsey Professor of Cell Biology and Anatomy. B.A. 1963, National College of Buenos Aires (Argentina); M.D. 1970, University of Buenos Aires (Argentina)

Roepe, Paul D., Assistant Professor of Molecular Pharmacology and Therapeutics. B.A. 1982, M.A. 1984, Ph.D. 1987, Boston University

Rosen, Neal, Associate Professor of Cell Biology and Genetics, Associate Professor of Medicine. A.B. 1971, Columbia College; M.D., Ph.D. 1979, Albert Einstein College of Medicine

Rothman, James E., Professor of Cell Biology and Genetics. B.A. 1971, Yale College; Ph.D. 1976, Harvard Medical School

Rottenberg, David A., Adjunct Professor of Neuroscience and Neurology (University of Minnesota). B.A. 1963, University of Michigan; M.Sc. 1967, University of Cambridge (United Kingdom); M.D. 1969, Harvard University

Rubin, Albert L., Professor of Biochemistry. Professor of Surgery. Professor of Medicine. M.D. 1950, Cornell University Medical College

Ruggiero, David A., Associate Research Professor of Neuroscience. B.A. 1972, Queens College of the City University of New York; M.A. 1976, M.Phil. 1977, Ph.D. 1977, Columbia University

Russo, Carlo, Associate Research Professor of Immunology in Medicine. M.D. 1977, University of Genova Medical School (Italy)

Sackin, Henry J., Associate Professor of Physiology and Biophysics. B.A., B.S. 1970, M.S. 1971, Brown University; Ph.D. 1978, Yale University

Salmon, Jane Eva, Associate Professor of Medicine. A.B. 1972, New York University; M.D. 1978, College of Physicians and Surgeons, Columbia University

Santos-Buch, Charles A., Professor of Pathology. A.B. 1953, Harvard University; M.D. 1957, Cornell University Medical College

Saxena, Brij B., Professor of Endocrinology in Obstetrics and Gynecology. Ph.D. 1954, University of Lucknow (India); D.Sc. 1957, University of Munster (Germany); Ph.D. 1961, University of Wisconsin

Scheinberg, David A., Associate Professor of Molecular Pharmacology and Therapeutics. A.B. 1977, Cornell University; M.D., Ph.D. 1983, Johns Hopkins University School of Medicine

Schwab, Rise, Associate Professor of Immunology in Medicine. B.S. 1971, State University of New York at Stony Brook; Ph.D. 1981, Cornell University

Schwartz, Morton K., Professor of Molecular Pharmacology and Therapeutics. B.A. 1948, Lehigh University; Ph.D. 1952, Boston University

Scotto, Anthony William, Associate Research Professor of Biochemistry in Medicine, Associate Research Professor of Biochemistry. B.A. 1969, C.W. Post College; M.S. 1970, Long Island University; Ph.D. 1978, St. John's University

Scotto, Kathleen Weihs, Assistant Professor of Molecular Pharmacology and Therapeutics. B.S. 1977, St. John's University; Ph.D. 1983, Cornell University Graduate School of Medical Sciences

Sealey, Jean E., Research Professor of Physiology and Biophysics. B.Sc. 1959, D.Sc. 1975, University of Glasgow (United Kingdom)

Senterfit, Laurence B., Professor of Microbiology. Professor of Pathology. B.S. 1949, M.S. 1950, University of Florida; Sc.D. 1955, Johns Hopkins University

Sheffery, Michael B., Associate Professor of Molecular Biology. A.B. 1975, M.S. 1977, Ph.D. 1981, Princeton University

Shuman, Stewart, Associate Professor of Molecular Biology. B.A. 1976, Wesleyan University; M.D., Ph.D. 1983, Albert Einstein College of Medicine

Silagi, Selma, Professor Emeritus of Genetics in Obstetrics and Gynecology. B.A. 1936, Hunter College of the City University of New York; M.A. 1938, Columbia University; Ph.D. 1961, Columbia University

Silverstein, Roy L., Associate Professor of Medicine. B.S. 1975, Brown University; M.D. 1979, Emory University School of Medicine

Sirlin, Julio L., Professor of Cell Biology and Anatomy. Professor of Cell Biology in Obstetrics and Gynecology. D.Sc. 1953, University of Buenos Aires (Argentina)

Sirotnak, Francis M., Professor of Molecular Pharmacology and Therapeutics. B.S. 1950, University of Scranton; M.S. 1952, University of New Hampshire; Ph.D. 1954, University of Maryland

Siskind, Gregory W., Professor of Medicine. B.A. 1955, Cornell University; M.D. 1959, New York University

Smith, Gerard P., Professor of Psychiatry. B.S. 1956, St. Joseph's College; M.D. 1960, University of Pennsylvania

Smith, Kendall A., Professor of Medicine. B.S. 1964, Denison University; M.D. 1968, The Ohio State University College of Medicine

Soffer, Richard L., Professor of Medicine. Professor of Biochemistry. B.A. 1954, Amherst College. M.D. 1958, Harvard University

Sonenberg, Martin, Professor of Cell Biology and Genetics. Professor of Medicine. B.S. 1941, University of Pennsylvania; M.D. 1944, Ph.D. 1952, New York University

Staiano-Coico, Lisa, Associate Professor of Microbiology in Surgery. B.S. 1976, Brooklyn College of the City University of New York; Ph.D. 1981, Cornell University Graduate School of Medical Sciences

Stenzel, Kurt H., Professor of Biochemistry. Professor of Surgery. Professor of Medicine. B.S. 1954, New York University; M.D. 1958, Cornell University Medical College

Stephenson, John L., Professor of Biomathematics in Physiology and Biophysics. B.A. 1943, Harvard University; M.D. 1949, University of Illinois

Sternberg, Stephen S., Professor of Molecular Pharmacology and Therapeutics. B.A. 1941, Colby College; M.D. 1944, New York University

Stoeckle, Mark Young, Assistant Professor of Medicine. Assistant Professor of Medicine in Microbiology. A.B. 1974, Harvard College; M.A., M.D. 1978, Harvard Medical School

Stokes, Peter E., Professor of Medicine, Professor of Psychiatry. B.S. 1948, Trinity College; M.D. 1952, Cornell University Medical College

Stutman, Osias, Professor of Immunology. B.A. 1950, Colegio Nacional Sarmiento (Argentina); M.D. 1957, Buenos Aires University Medical School (Argentina)

Sussdorf, Dieter H., Associate Dean, Associate Professor of Microbiology. B.A. 1952, University of Missouri; Ph.D. 1956, University of Chicago

Szeto, Hazel H., Associate Professor of Pharmacology. B.S. 1972, Indiana University; M.D. 1977, Cornell University Medical College; Ph.D. 1977, Cornell University Graduate School of Medical Sciences

Tate, Suresh S., Associate Professor of Biochemistry. B.Sc. 1958, M.Sc. 1960, University of Baroda (India); Ph.D. 1963, University of London (United Kingdom)

Tempst, Paul, Associate Professor of Molecular Biology. B.S. 1976, Ghent State University (Belgium); Ph.D. 1981, Ghent University (Belgium)

Townes-Anderson, Ellen, Associate Professor of Physiology and Biophysics. Associate Professor of Physiology in Ophthalmology. B.A. 1968, Connecticut College; M.A. 1971, University of California, Berkeley; Ph.D. 1980, Boston University School of Medicine

Traktman, Paula, Associate Professor of Cell Biology and Anatomy. Associate Professor of Cell Biology and Anatomy in Microbiology. A.B. 1974, Radcliffe College, Harvard University; Ph.D. 1981, Massachusetts Institute of Technology

Udenfriend, Sidney, Adjunct Professor of Biochemistry. B.S. 1939, City College of the City University of New York; M.S. 1942, Ph.D. 1948, New York University

Victor, Jonathan D., Professor of Neurology and Neuroscience. B.A. 1973, Harvard University; Ph.D. 1979, The Rockefeller University; M.D. 1980, Cornell University Medical College

Volpe, Bruce T., Associate Professor of Neurology and Neuroscience. B.S. 1969, Yale College; M.D. 1973, Yale University School of Medicine

Wagner, John Anthony, Professor of Neurology and Neuroscience. Professor of Cell Biology and Anatomy. B.S. 1970, Loras College; Ph.D. 1975, Princeton University

Wahlestedt, Claes R., Assistant Professor of Neuroscience. M.D. 1984, Ph.D. 1987, University of Lund (Sweden)

Watanabe, Kyoichi A., Professor of Molecular Pharmacology and Therapeutics. Ph.D. 1963, Hokkaido University (Japan)

Weinstein, Alan M., Associate Professor of Physiology and Biophysics. Associate Professor of Medicine. A.B. 1971, Princeton University; M.D. 1975, Harvard University

Weksler, Babette B., Professor of Medicine. B.A. 1958, Swarthmore College; M.D. 1963, Columbia University

Weksler, Marc E., The Irving Sherwood Wright Professor of Geriatrics in Medicine. B.A. 1958, Swarthmore College; M.D. 1962, Columbia University

Wellner, Daniel, Associate Professor of Biochemistry. A.B. 1956, Harvard University; Ph.D. 1961, Tufts University

White, Perrin C., Associate Professor of Pediatrics. A.B. 1972, Harvard University; M.D. 1976, Harvard Medical School

Wiedmann, Martin, Assistant Professor of Cell Biology and Genetics. Diplom 1975, University of Greifswald (Germany); Ph.D. 1979, University of Potsdam (Germany)

Windhager, Erich E., The Maxwell M. Upson Professor of Physiology and Biophysics. M.D. 1954, University of Vienna (Austria)

Yang, Soo Young, Associate Professor of Immunology. M.S. 1972, Minnesota State University; Ph.D. 1981, New York University

Zakim, David, The Vincent Astor Distinguished Professor of Medicine. B.A. 1956, Cornell University; M.D. 1961, State University of New York Downstate Medical Center

Zelenetz, Andrew, Assistant Professor of Molecular Biology. A.B. 1977, Harvard University; M.D., Ph.D. 1984, Harvard Medical School

Degree Recipients 1992–93

Doctors of Philosophy

Becker, Murray David, B.A. 1985, University of Chicago; Physiology and Biophysics, Professor Olaf S. Andersen. Thesis: "Amino Acid Sequence Modulation of Gramicidin Channel Function: Effects of Tryptophan-to-Phenylalanine Substitutions on the Single-Channel Conductance and Duration."

Cheng, Peter Y., B.A. 1986, Cornell University, M.S. 1988, Tufts University; Pharmacology, Professor Hazel Szeto. Thesis: "The Role of mu-1 and Delta Opiate Receptors in the Modulation of Fetal Respiratory Activity."

Cho, Sunghee, B.S. 1979, Yonsei University (Korea); Neuroscience, Professor William Pulsinelli. Thesis: "Molecular mechanism(s) of Ischemic Neuronal Injury: The Role of Excitatory Amino Acids Neurotransmitters and Receptors."

Claude, Alejandro A., M.S. 1987, Universidad Catolica (Chile); Molecular Biology, Professor Jerard Hurwitz. Thesis: Isolation and Characterization of an RNA Helicase and the Cloning of a Putative RNA Helicase from HeLa cells."

de Bruin, Derik, B.S. 1986, Eastern New Mexico University; Molecular Biology, Professor Jeffrey Ravetch. Thesis: "Structural and Transcriptional Characterization of *Plasmodium falciparum* Chromosomes."

DiMartino, Jorge F., B.A. 1985, University of California, Berkeley; Immunology, Professor Janet S. Lee. Thesis: "Novel Cis-acting Elements Regulate Expression of CD-45."

Edwalds-Gilbert, Gretchen Marie, B.A. 1982, Swarthmore College; Molecular Biology, Professor Erik Falck-Pedersen. Thesis: "The Role of Processing Signals in Transcription Termination by RNA Polymerase II."

Eisenberg, Carol Ann, B.S./B.A. 1981, Cabrini College, M.S. 1983, Villanova University; Cell Biology and Genetics, Professor David Bader. Thesis: "Derivation and Characterization of an Embryonic Quail Mesoderm Cell Line and Analysis of its Cardiogenic Potential."

Hagler, Jeremiah Cadick, B.A. 1987, University of California, Santa Cruz; Molecular Biology, Professor Stewart Shuman. Thesis: "In Vitro Analysis of Vaccinia Virus Early Transcription."

Huang, Chin-shiou, B.S. 1982, Kaohsiung Medical College, M.S. 1984 National Tsinghua University (Republic of China); Biochemistry, Professor Alton Meister. Thesis: "Regulation of γ-Glutamylcysteine Synthetase and its Subunit Structure."

Huang, Eric Jinsheng, B.M. 1986, National Taiwan University (Republic of China); Molecular Biology, Professor Peter Besmer. Thesis "Genetic Analysis and Biochemical Characterization of the c-kit Receptor Ligand: A Pleiotropic Growth Factor Encoded by the Murine Steel Locus."

Huang, Hsien-bin, B.S. 1984, M.S. 1986, National Taiwan Normal University (Republic of China); Biochemistry, Professor Esther Breslow. Thesis: "Studies of Folding and Allosteric Mechanisms in Neurophysin."

Kane, Eileen Marie, B.A. 1985, Hunter College; Molecular Biology, Professor Stewart Shuman. Thesis: "Vaccinia Virus Transcription: Analysis Utilizing Temperature-Sensitive Mutant Viruses and Antiviral Drugs."

Lander, Harry Michael, B.S. 1987, State University of New York at Stony Brook; Biochemistry, Professor Kurt H. Stenzel., Thesis: "Stress Stimuli-Induced Lymphocyte Activation."

Lee, Jin-Moo, B.A. 1985, Yale University; Neuroscience, Professor Ira B. Black. Thesis: "Characterization and Purification of a Neuronal Differentiation Factor."

Li, Mingxia, B.S. 1982, Beijing Second Medical College (People's Republic of China); M.S. 1985, Chinese Academy of Medical Sciences; Pharmacology, Professor Joseph R. Bertino. Thesis: "Development of Methotrexate Resistance in Mice by Retroviral Gene Transfer of Altered DHFR Gene."

Lim, Lorena Carlos, B.S. 1979, University of the Philippines at Los Banos; Molecular Biology, Professor Michael Sheffery. Thesis: Cloning and Characterization of the Eukaryotic Transcription Factor CP2."

Liu, Su, M.D. 1982, Shanghai First Medical College (People's Republic of China); Molecular Biology, Professor Joseph R. Jack. Thesis: "Genetic Characterization of the Cut Gene and its Regulatory Role in Cell Type Specification."

McDonald, William, B.A. 1985, University of Florida; Cell Biology and Genetics, Professor Paula Traktman. Thesis: "The Vaccinia Virus DNA Polymerase: Regulated Expression and Enzymology."

Mahajan, Rohit Kumar, B.A. 1984, Swarthmore College; Cell Biology and Genetics, Professor Joel D. Pardee. Thesis: "A Mechanism of Myosin Assembly and Regulated Formation of Contractile Fibers in Dictyostelium Amoebae."

Muench, Marcus, B.S. 1986, University of California, Davis; Cell Biology and Genetics, Professor Malcolm A.S. Moore. Thesis: "Cytokine Interactions in the Regulation of Primitive Murine Hematopoietic Progenitors."

Onrust, Rene, B.S. 1983, M.S. 1985, University of Aukland (New Zealand); Molecular Biology, Professor Michael O'Donnell. Thesis: "The Structure and Function of the Accessory Proteins of the *E. coli* DNA Polymerase III Holoenzyme."

Roy, Nita, B.A. 1987, Hood College; Molecular Biology, Professor Eli Gilboa. Thesis "Generation of Influenza-Specific Cytotoxic T-Lymphocytes Using Retroviral Gene Transfer."

Sherwood, Peter Willet, B.S. 1985, Cornell University; Molecular Biology, Professor Mary Ann Osley. Thesis: "Histone Gene Regulation in Saccharomyces Cerevisiae."

Szabó, Anikó, M.D. 1982, Szeged University Medical School (Hungary); Neuroscience, Professor Henry Furneaux. Thesis: "Cloning and Characterization of HuD: A Human Brain Paraneoplastic Antigen."

Tantravahi, JogiRaju Venkata, B.A. 1984, Columbia University; Molecular Biology, Professor Erik Falck-Pedersen. Thesis: "Characterization of RNA Polymerase II Transcription Termination Regions from the Mouse B^{MAJ} Globin Gene and the Adenovirus Major Late Transcription Unit."

Vodovotz, Yoram, B.S. 1988, University of Wisconsin, Madison; Immunology, Professor Carl Nathan. Thesis: "Suppression of Macrophage Effector Functions by Macrophage Deactivating Factor, Transforming Growth Factor-ß, Interleukins-4 and -10, and Bacterial Lipopolysaccharide."

Zebala, John Anthony, B.S. 1986, University of Southern California; Molecular Biology, Professor Francis Barany. Thesis: "DNA Recognition of Base-Analogue and Chemically Modified Substrates by the TaqI Restriction Endonuclease."

Zhu, Yuan-Shan, B.A. 1978, M.D. 1982, Hunan Medical College (People's Republic of China); Pharmacology, Professor Charles Inturrisi. Thesis: Differential Regulation of c-fos Proenkephalin and Tyrosine Hydroxylase Gene Expression in the Rat Adrenal."

Masters of Science

Cho, Jaeyoung, B.S. 1988, Pusan National University (Korea); Neuroscience, Professor Harriet Baker. Thesis: "Peripheral Afferent Regulation of Tyrosine Hydroxylase Regulation in Adult Rats."

Martinez, Juan A., B.S. 1990, Tulane University; Physiology and Biophysics, Professor Bernice Grafstein. Thesis: "Studies on the Release of Soluble Extra-Cellular Glycoproteins (X-GPs) from Goldfish Optic Tectum and Optic Nerve."

Tumang, Maria C. Tancinco, B.S. 1988, State University of New York at Stony Brook; Immunology, Professor Henry W. Murray. Thesis: "The Role and Effect of Tumor Necrosis Factor -α in Experimenting Visceral Leishmaniasis."

Students 1993-94

Candidates for the Degree of Doctor of Philosophy

Entering Students

Atherton, Ruth Elizabeth (Cell Biology and Genetics). B.A. 1993, University of California, Santa Barbara. Portland, Oregon

Baldwin, Michael (Molecular Biology). B.A./B.S. 1993, State University of New York, Binghamton. Massapequa, New York

Basu, Subham (Pharmacology). B.A. 1991, University of California, Berkeley. Noamundi, India

Bennett, Richard Lynn (Molecular Biology). B.A. 1993, Kalamazoo College. Detroit, Michigan

Bradsher, John Norman (Molecular Biology). B.S. 1989, Oklahoma Baptist University; M.S. 1990, University of Oklahoma. Broken Arrow, Oklahoma

Broomleigh, Virginia Carrington (Cell Biology and Genetics). B.A. 1987, M.S. 1990, New York University. Anaheim, California

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